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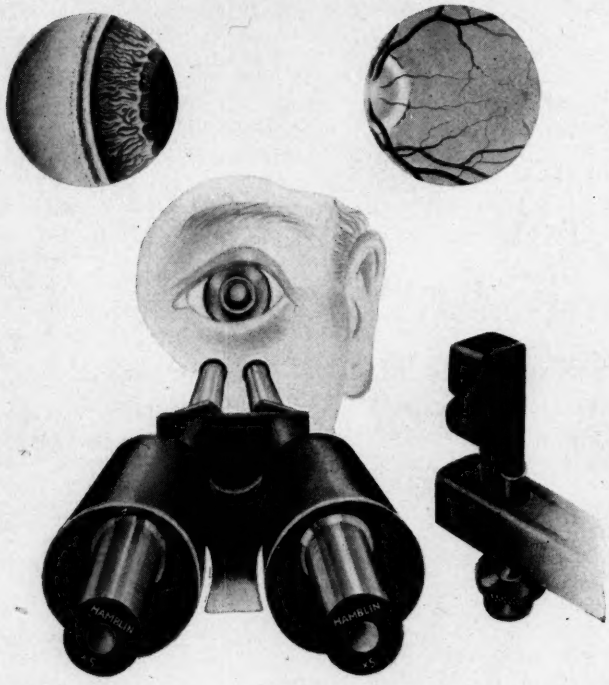

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Brit. J. Ophthal. (1954) 38, 641.

COMMUNICATIONS

IRIDENCLEISIS IN CONGESTIVE GLAUCOMA*

BY

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IN 1945–46 one of us (EGM) became aware that approximately 20 years in ophthalmology had not taught how or why the classical von Graefe iridectomy deserved its pride of place in the surgical treatment of acute (congestive) glaucoma; nor did any authority pretend to this knowledge. The operative results were not outstandingly commendable and congestive glaucoma remained a condition of serious prognosis for vision. On the contrary a considerable experience of Holth iridencleisis in " chronic " glaucoma had shown far better results which might be due either to the character of the operation or, more probably, to the state of the eye at the time of surgical intervention.

Numerous attempts to systematize various types of glaucoma from the surgical point of view and to draw logical conclusions as to the rational operative procedure in each particular case did not seem to yield unequivocal directives for the surgeon confronted with his patient. The surgical approach to glaucoma was first suggested by von Graefe (1859) as an empirical measure, and it is on this empirical basis that we still stand to-day. The " theoretical " objections to the mere idea of an operation on a congested eye were very strong, and more than 40 years after von Graefe's publication de Wecker (1901) thought it important to devote a great part of his lecture on iridectomy in glaucoma to opposing the prejudice against it.

When the mechanism of the rise in ocular tension is clinically obvious, the choice of treatment is also obvious: iridectomy in secondary glaucoma with seclusio pupillae, Barkan's goniotomy in congenital malformations of the angle of the anterior chamber, and so on. In cases of primary idiopathic glaucoma—be it narrow or wide angle or of the over-secretive or impeded-drainage type—the choice of procedure is usually determined by the surgeon's experience with various techniques or his operative routine.

In congestive glaucoma it is less possible than in any other form to decide the choice of operation from the clinical picture, and in most clinics a routine operation is performed unless contraindicated.

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Rationale of Operation for Congestive Glaucoma

Before 1946 it had become abundantly clear that some advantage to chronic cases was gained in iridencleisis by early closure of the scar with quick re-formation of the anterior chamber. This reduces the incidence of haemorrhages from sudden decompression and loss of external support to arteries in a state of relative vasodilation or vasomotor laxity. It seemed that if this decreased incidence of haemorrhage occurred in the "quiet" eye of the chronic glaucoma case, it might be found even more useful in the eye in a state of active congestion.

The recommended technique for the von Graefe operation involves a broad iridectomy with tearing away of the iris root. To von Graefe the breadth of the iridectomy meant a diminution of the surface capable of producing aqueous. "Opening up of the angle" and some dramatic interruption of disordered vasomotor reflexes were suggested by others as possible mechanisms.

These same purposes might be achieved equally well in the course of the iridencleisis operation if this were used for congestive cases, and this would leave the eye with an incarcerated iris and the mechanical basis for a permanent filtering scar if the post-operative tension of the eye should require it. In such a concept the element of self-regulation in the Holth operation is a valuable factor—the intraocular pressure itself determining the amount of filtering or fluid shift along the iris wick into the subconjunctival tissues.

The technique would require a small modification of the simple Holth operation, in that, after the section of the iris sphincter and down to the iris root, the pillar left in the grasp of the forceps should be pulled sideways so as to tear a little of the iris root. It is only then incarcerated—hence the keratome incision should be enlarged slightly in its total width to allow this manoeuvre.

A certain reserve was felt on the possible effects of opening up subconjunctival channels in the congested eye, but in practice no difficulty was found.

The routine use of this operation was established and favourable experience led to its continuation.

At a later stage one of us (KR) adopted the *ab externo* approach to the original Holth technique (Schlösser, 1922) as a measure of safety which is undoubtedly promoted by this cautious method. In theory, the creation of a conjunctival flap with a wide area of subsequent scar tissue might be thought inimical to the spread and absorption of aqueous. In practice no appreciable disadvantage of this kind was noted. The slight extension of recovery time by comparison with that experienced with the simple Holth approach is a small price to pay for security.

The material now justifies a review of the results and the statistics provoke certain reflections.

Historical Survey

The literature contains little material on the surgical treatment of congestive glaucoma, and many accounts of glaucoma surgery do not single out the results obtained in congestive cases. Table I (opposite) is collected from various reports in the literature. The percentages of success in most of these reports are based on such small numbers of operated cases as to have no real meaning. By grouping these reports according to the type of operation performed and summing up the results,

TABLE I

SURGICAL TREATMENT OF CONGESTIVE GLAUCOMA

Author	Date	No. of Cases	Operation	Percentage Success	Remarks
Sulzer	1901	113	Iridectomy	full 21 part 34	16 total blindness
Koster Gzn	1906	222	Iridectomy	full 45 part 27	
Vettiger	1901	?	Iridectomy	full 74 part 4	
Meller	1914	47	Lagrange	95	Two failures in 178 chronics
		19	Elliott	100	
Gunnufsen	1916	9	Iridectomy	11	amongst 130 chronics
Sattler	1921	?	Elliott	83	amongst 429 chronics
Whitehead	1927	38	Iridectomy	full 57·9 part 26·3	
Holth	1927	3	Iridencleisis	100	
Spaeth	1928	16	Iridectomy		
Pillat	1928	11	Iridencleisis	90	
Holth	1930	6	Iridencleisis	100	
Gjessing	1931	1	Iridencleisis	100	amongst 122 chronics
Löfgren	1932	11	Elliott	73	amongst 247 chronics
		47	Iridectomy	81	
		2	Iridencleisis	100	
Butler	1932	12	Iridencleisis	83	
		26	Elliott	54	
Ploman and Granström	1932		Iridectomy	60	
Clapp	1934	6	Iridencleisis	100	
Lloyd	1948	19	Iridectomy	full 42 part 15	
		4	Iridencleisis	100	

a more reliable picture may be obtained. This is done in Table II (overleaf), which shows that iridectomy, which is—we believe—performed by most surgeons as the operation of choice in congestive glaucoma, yields results that are far from satisfactory; Duke-Elder (1940) writes that . . . . " a good average for successes in acute

glaucoma is 60 per cent.". Sclerectomy operations—Lagrange and Elliott's types—proved to be dangerous in congestive cases, and are not practised nowadays, although it is not quite clear why the Lagrange operation was discarded. It may have dropped out of use for this condition because it had a relatively limited vogue, tending to be overshadowed by the corneo-scleral trephining of Elliott. The number of iridencleisis operations performed in congestive cases must considerably exceed the figures cited above. Holth (1933) stated that since 1916 all his acute cases had been treated with iridencleisis; Lindner (1939) stated that in his clinic in Vienna iridencleisis had been performed as a routine for all glaucomas since 1921 unless contraindicated; but detailed reports are lacking.

TABLE II

SURGICAL TREATMENT OF CONGESTIVE GLAUCOMA

Operation	No. of Cases	Percentage Success	Remarks
Iridectomy	264	49	Plus 21 " partial " (sum 70)
Lagrange	47	95	Meller's material only
Elliott	68	77	
Iridencleisis	43	96	

Selection and Management of Cases now Reported

In the years 1946–1954, 110 consecutive cases of congestive glaucoma (65 females and 45 males) were operated upon (Table III). The patients were admitted to hospital as emergencies and medical treatment was started at once. This consisted of " intensive Eserine " (1 drop of 0·5 per cent. solution every 5 min. for 30 min., followed by 1 drop every 30 min. until the tension was reduced and the pupil contracted), $\frac{1}{8}$ to $\frac{1}{4}$ gr. morphine by hypodermic, and two leeches applied to the temple. Next day (*i.e.* within 12 to 24 hours) iridencleisis was performed. Cases which fully responded to medication are not included in this report. We are unable to state in exactly how many cases the tension was reduced to normal or nearly normal by medical means, but all eyes in this series were in a state of congestion at the time of operation. The ordinary Holth approach was used in 34 cases, the *ab externo* approach in 76. The eyes were treated with gutt. homatropine 1 per cent. three times a day for 3 days after operation, and the patients were discharged as a rule after 5 days on gutt. pilocarpine 1 per cent. three times a day with instructions to massage the eye.

TABLE III

DISTRIBUTION OF CASES

Year	1946	1947	1948	1949	1950	1951	1952	1953	1954
No. of Cases	1	8	22	22	16	20	8	15	1

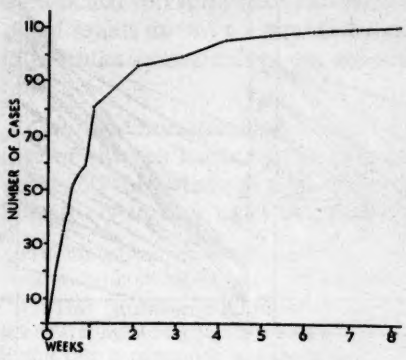

FIG. 1.—Rate of hospitalization of congestive glaucoma cases. In ten cases the information was considered unreliable and they are not included.

Duration of Attack.—Our findings here agree with those of Lloyd (1948): an attack of congestive glaucoma is not always considered by the patient to be an emergency. The range of duration of attack before seeking medical advice in this series was between 6 hours and 8 weeks, but 70 per cent. of the cases entered hospital within the first week (Fig. 1).

Observation Time after Operation.—No case in this report was operated upon less than 4 months ago, seven cases only were operated upon within the past 12 months. Sixteen cases were operated upon 3 to 5 years ago, but ceased attending the glaucoma clinic after a few months, considering themselves cured; these are included under the short observation time group (Table IV).

TABLE IV

OBSERVATION TIME (YEARS)

Observation Time	Less than 1	1–2	2–4	4–6	6–8
No. of Cases	23	22	29	22	12

Results

To establish the efficiency of an antiglaucoma operation it is clearly necessary to estimate three factors: influence on visual field, influence on visual acuity, and control of intra-ocular pressure. In cases of congestive glaucoma this would be unobtainable. Visual field plotting is not practicable during the attack and the visual acuity is reduced by raised tension and a steamy cornea, as well as by the general state of the patient who cannot be made to co-operate. Only the intra-ocular pressure can be estimated and compared with the post-operative state.

Visual Acuity.—The dramatic post-operative improvement of visual acuity should be considered the rule rather than the exception in congestive cases. The results obtained by us are set out in Fig. 2 (overleaf) for the purpose of completeness of this report but are not considered an achievement.

A history of previous congestive attacks was given by 27 patients whose visual prognosis is worse than that of those suffering from first attacks (Fig. 2B), undoubtedly because of gradual deterioration of vision during the glaucomatous state before attendance.

First attacks in a previously good eye were suffered by sixty patients (uncomplicated, primary cases only are included here). Fig. 3 (overleaf) records an attempt to ascertain the influence of the delay in relieving the

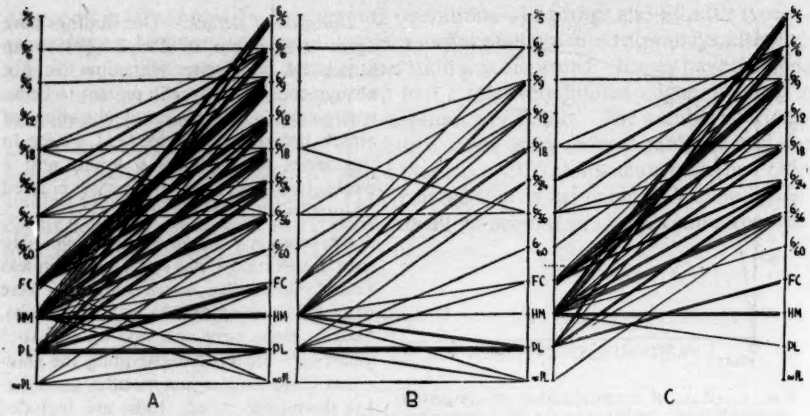

FIG. 2.—Comparison of pre- and post-operative visual acuity in 110 cases of congestive glaucoma.
A: whole series;
B: 27 cases who had had " previous attacks ";
C: Sixty cases of " primary attack ".

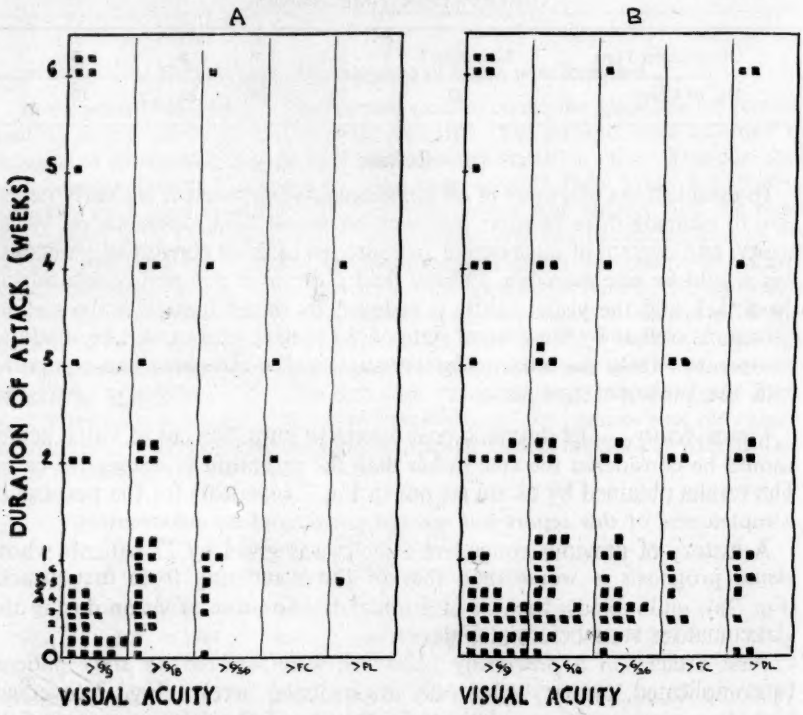

FIG. 3.—Final visual acuity in relation to duration of congestive attack.
A: " primary attack " only (sixty cases), amblyopia, thrombosis, retinopathy and lens sclerosis are excluded;
B: whole series.

intra-ocular pressure (delayed attendance) on final visual acuity. Good visual results do not go hand-in-hand with immediate operation, and raised intra-ocular pressure does not affect central visual acuity for a considerable time.

Control of Intra-Ocular Pressure.—Excluding nine thrombotic cases and one case of vitreous haemorrhage on entering the anterior chamber, which was very likely thrombotic as well, the intra-ocular pressure remained raised post-operatively in four cases (4 per cent.).

(1) This patient had a subluxated lens—noted post-operatively—which was subsequently removed without influence on the raised tension.

(2) This patient gave a history of previous attacks in both eyes, was admitted with bilateral congestive glaucoma, and did not respond to medication at all; final visual acuity in this case is perception of light in each eye.

(3) This patient gave a history of recurrent attacks for the previous 2 years, cataracts were present in both eyes, and the other eye was affected by absolute glaucoma; subsequent cataract extraction was followed by uveitis, and the final visual acuity was perception of light.

(4) This patient attended after 2 weeks after the onset of pain, and medication had no effect on the tension; there was a history of many previous attacks, and the optic discs were cupped. His visual acuity of 6/18 has remained unchanged for the past 12 months, his visual field is small (20°), and the tension is 35 mm. Hg Schiötz in a white eye. It has been decided to perform a cyclodialysis on this eye in the near future.

In two further cases (2 per cent.) the tension remained full (about 30 mm. Hg Schiötz). One was operated upon 14 months ago, the other 4 years ago. Their visual acuity is 6/9 and 6/12 respectively since operation with full visual fields and no complaint, and we do not propose to interfere with these eyes.

The lowering of tension was delayed in six cases (6 per cent.), in five of which the tension was raised after operation for 2 to 8 weeks before becoming normal. The visual acuity and visual fields of these cases did not deteriorate during this time.

One eye developed post-operative hypotension which lasted for 4 weeks. Visual acuity in this case deteriorated from a post-operative 6/18 to hand movements. There were no keratic precipitates or cloudiness of the media or any other signs of uveitis.

Pre-Operative Complications

Thrombotic Glaucoma.—There were five cases of central vein occlusion and four of occlusion of one of the two main branches.

The visual results in the first group are: two hand movements, one perception of light, and two enucleated; in one case only did the intra-ocular pressure eventually come down to normal.

In the four incomplete occlusions, the visual results were 6/36, 4/60, hand movements, and perception of light. In three of these cases the tension was controlled by the operation, in one it remained full (30 mm. Hg Schiötz).

As would be expected, iridencleisis—like the other filtering operations—is of little avail in thrombotic glaucoma. These nine cases were operated upon only because of diagnostic difficulties in the acute stage.

Hypertensive Retinopathy.—In three cases hypertensive retinopathy was diagnosed post-operatively; they finished with a visual acuity 6/6, 6/18, and 6/24 respectively, and controlled tension.

Central Artery Occlusion.—In one case an old occlusion of the central artery was diagnosed post-operatively. The tension was controlled and the visual acuity in the remaining field was hand movements.

Diabetes.—There were four diabetics in these series.

Two of them belong to the thrombotic group and developed vitreous haemorrhage, the eyes being subsequently enucleated.

Of the other two, one had an orbital haemorrhage when retrobulbar novocaine was being injected before operation, and iridencleisis had to be preceded by posterior sclerotomy; the final visual acuity in this case is 6/9. The second patient was admitted with intumescent cataract; iridencleisis resulted in a quiet eye with normal tension, but subsequent cataract extraction revealed post-uveitic dystrophy of the fundus and secondary optic atrophy; the visual acuity is now perception of light.

State of the Other Eye.—In thirty cases the other eye was already affected by glaucoma. In eight of these it was in a state of absolute glaucoma on admission; in two cases chronic glaucoma was confirmed by typical visual field changes; in twenty cases the following antiglaucoma operations had been performed on the other eye before the present attack:

Iridencleisis	15
Iridectomy	2
Elliott's trephine	2
Cyclodialysis	1

Five patients were admitted with bilateral congestive attacks and both eyes were operated on at the same session. Three further cases were bilateral, but the attack affected each eye on different occasions.

These figures are worth noting in view of recent attempts to differentiate between patients whose eyes are affected by simple glaucoma, and those who (it is suggested) never develop a congestive episode and *vice versa* (Lloyd, 1948). Our material does not support this view.

Operative and Post-Operative Complications

Iris Rigidity.—The iris proved rigid and the inclusion of a pillar impossible in two cases of congestive glaucoma. Basal iridectomy was performed instead of iridencleisis and these cases are not included in the present study. A rigid and fibrous iris was met more often in chronic cases; in congestive cases it does not seem to present a problem.

Hyphaema.—Occurrence of hyphaema is common at the moment of cutting through the sphincter, but we are unable to give exact figures for its incidence. In no case did it fail to resorb without trace and without any influence on the final result.

Vitreous Haemorrhage.—In four cases, vitreous haemorrhage occurred on entering the anterior chamber.

Two were diabetic cases and they lost their eyes (*vide supra*).

The third was a case of central vein occlusion, in which the intra-ocular pressure settled down to normal and the visual acuity to hand movements.

The fourth was a case of glaucoma in an aphakic eye with no perception of light.

Late Infection.—One eye became purulent 3 months after operation, went into phthisis bulbi, and was enucleated 3 years later.

Uveitis.—Two cases fall into this group.

The first eye developed keratic precipitates after operation, the tension persisted high, the cornea did not recover from bullous degeneration with which the patient was admitted, and the visual acuity was perception of light. The other eye was not affected. This patient had very bad dental sepsis which he refused to have treated.

The second patient was admitted with fine keratic precipitates in the eye affected by congestive glaucoma but with a wide pupil. It was decided to operate, but the eye did not settle down, and 2 months after operation keratic precipitates were present in both eyes. Eventually the eyes became quiet and secondary cataract was extracted from one of them, giving the patient a visual acuity of 6/9 with correction.

Luxation of Lens.—Two cases fall into this group.

In one the lens was found subluxated after operation, and was successfully extracted, but the tension persists elevated in a quiet eye.

In the second case, the lens was found lodged in the vitreous when the patient attended the department 1 year after operation complaining of sudden onset of blurred vision. No attempt was made at extraction; the visual acuity in this eye is 6/6 with correction (since 1948), and the tension remains normal.

Sympathetic Ophthalmia

Two female patients developed sympathetic ophthalmia, presenting a classical clinical picture including poliosis in one case. In both the condition was diagnosed 9 weeks after operation which was uneventful and resulted at first in a quiet eye with normal tension and visual acuities of 6/6 and 6/60 respectively. In spite of vigorous treatment, which included arsenicals, cortisone, protein shock therapy, and anti-

TABLE V

INCIDENCE OF SYMPATHETIC OPHTHALMIA IN IRIDENCLEISIS

Author	Year	No. of Cases	Percentage of Symptoms	Remarks
Gunnufsen	1916	127	none	36 cases only followed
Galetski-Olin	1922	20	none	
Gjessing	1927	113	none	92 cases only followed
Gjessing	1931	122	none	
Hagen	1932	175	none	
Holth	1933	221	none	
Holst	1934	534	1	
Gjessing	1939	198	none	All chronics
Goar and Schultz	1939	?	none	
Reid	1940	100	none	All chronics
Butler	1940	100	none	
Iliff	1943	47	1	Negro patients only
Mackie	1948	100	none	
Lloyd	1948	6	none	All congestive

biotics, these cases fared badly. Final visual acuity in the first case became 6/36 in the better eye and in the second case no perception of light and phthisis bulbi were the result (This is the only case of complete blindness in this series).

Because sympathetic ophthalmia is the mainstay of all criticism of iridencleisis, it seems essential to attempt to ascertain its incidence. The reports of various authors practising iridencleisis are set out in Table V. The percentages and numbers of cases apply to all iridencleisis operations, that is, in chronic as well as in acute cases as it proved impossible to select the figures relating to congestive cases only.

These reports are very good but they are rather surprising. Sympathetic ophthalmia may occur after any intra-ocular operation, including iridencleisis, and Table VI shows its incidence in various conditions.

TABLE VI

INCIDENCE OF SYMPATHETIC OPHTHALMIA

Author	Date	Place	Total No. of Cases	Condition in which Sympathetic Ophthalmia arose						
				Penetrating Wounds	Cataract Operation	Other Intra-ocular Operation	Subconjunctival Scleral Rupture	Perforating Corneal Ulcer	Phthisis Bulbi	Intra-ocular Tumour
Fuchs	1905	Vienna	35	19	4	4	2	3	—	3
Grósz	1926	Budapest	156	141	11	4				
Theobald	1930	Illinois Eye Infirmary	11	8	2	1				
Joy	1935	New York State Survey	151	26	5	3	4	1	1	1
Verhoeff	1936	Massachusetts Eye Infirmary	35	20	7	7	—	1	—	—
Woods	1936	Wilmer Institute	28	23	2	1	1	1	—	—
Samuels	1936	New York State Survey	112	—	—	13	—	—	—	—
Irvine	1940	Massachusetts Eye Infirmary	63	—	11	11	—	—	—	—
McPherson	1949	Wilmer Institute	61	36	10	10	3	1	—	—
Total ...	...	... ...	652	273	52	54	10	7	1	4

The figures obtained for "other intra-ocular operations" are of special interest; not all authors specify what are the "other operations", but the available particulars (Table VII) show that all or nearly all "other operations" mean various antiglaucoma procedures. This connection is so well established that Samuels (1936) attempted a possible direct link between glaucoma itself and sympathetic ophthalmia.

TABLE VII

SYMPATHETIC OPHTHALMIA AFTER OPERATIONS OTHER THAN CATARACT EXTRACTION

Operation	Grósz (1926)	Verhoeff (1936)	Samuels (1936)	Irvine (1940)
Iridotasis		4		5
Iridectomy	3	2	4	5
Trephine	1	1	1	1
Cyclodialysis and posterior sclerotomy			1	

The fact that in all reviewed reports on iridencleisis—with two exceptions (Holst, 1934; Iliff, 1943)—sympathetic ophthalmia is not listed amongst complications may be explained only by erroneous diagnosis or by reasons more personal than surgical. The pathological reports show that sympathetic ophthalmia is rather over- than under-diagnosed clinically. Theobald (1930) could confirm the diagnosis histologically in only eleven out of 23 eyes enucleated because of the full clinical picture of "sympathetic"; McPherson (1949) confirmed only 25 out of 61 cases; Irvine (1940) only 37 out of 63 cases.

Regarding the deep-rooted abhorrence of calling a case of bilateral uveitis "sympathetic ophthalmia", certain relatively recent American surveys may be significant:

(1) Joy (1935) circularized 471 ophthalmologists in the state of New York asking about their experience with sympathetic ophthalmia. Only 212 of them replied; 112 of those denied having seen a case, eighteen admitted having seen some cases but were unable to supply any records, and the remaining 82 (19·5 per cent.) reported 151 cases.

(2) Haik, Waugh, and Lyda (1952) circularized 58 ophthalmologists seeking information on sympathetic ophthalmia and experience with cortisone in this condition; 29 replies denied having seen any cases, but the other 29 ophthalmologists supplied data of 69 patients in whom cortisone was used for sympathetic ophthalmia.

With due respect to these reports, we believe—and our experience bears it out—that sympathetic ophthalmia is a rare but classical complication of any intra-ocular operation, that it will continue to occur until its aetiology is elucidated and prevention made possible, and that it is only a matter of time before any surgeon encounters a case or cases. We had two cases of sympathetic ophthalmia in this series but taking our results as a whole we are not alarmed by this incidence.

Comment

The iridencleisis operation in congestive glaucoma has the following advantages:

(*a*) It is a one-stage operation assuring permanent drainage and normal intra-ocular tension.

Classical iridectomy in these cases aims only at termination of the attack; it is not supposed to and it does not effect a permanent surgical cure. Table II demonstrates that it yields a very modest percentage of success, and Table VII that it is not free from dangers.

(*b*) It is a safe operation, and the complications are few.

(*c*) It controls the tension. Of our four cases in which it failed to do so, the dislocated lens was probably produced by faulty technique; this leaves only 3 per cent. of failures, all in very advanced cases affected by repeated attacks. Hypotony on the other hand occurred in one case only.

(*d*) It is a quick and easy operation. Surgical emergencies—such as congestive glaucoma—have often to be operated on by intermediate grade staff, and possibly even by juniors; even in cases of very shallow anterior chamber the *ab externo* approach ensures safety.

(*e*) Recovery time after operation is shorter than after any other filtering operation because the trauma to the eye is slight.

The only point that might be advanced against iridencleisis seems to be the occasional occurrence of sympathetic ophthalmia. Our two cases (1·9 per cent.) could be fitted into previously quoted reports (Table V). The danger then seems to be very small, but even taking our statistics alone, it is open to discussion whether this experience—only one case of blindness amongst 110 patients affected by and operated on for congestive glaucoma—in any way outweighs all the other advantages of the operation.

Summary

110 cases of congestive glaucoma treated by a slightly modified Holth iridencleisis are described. The results appear to show a significant advantage over those obtained in this condition by the classical iridectomy.

We wish to thank Miss. E. Hatherley for kind permission to include her private and hospital patients in this report.

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DEGENERATIONS OF THE DOG RETINA*

VI. CENTRAL PROGRESSIVE ATROPHY WITH PIGMENT EPITHELIAL DYSTROPHY

BY

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THIS syndrome of central progressive atrophy of the retina in which central vision is lost in middle age while peripheral vision is retained until old age is unlike the generalized degenerations of the dog retina described in the preceding papers of this series, in two principal particulars: the distribution of the degeneration and the occurrence in the fundus of pigment foci which may be seen with the ophthalmoscope.

The syndrome was first recognized clinically when small foci of irregular pigmentation were observed in the tapetal fundus of dogs with a history of very gradual bilateral impairment of day and night vision coming on in middle or late life. The impairment of vision was due to the development of a central scotoma; the day and night vision of the peripheral fundus remained unimpaired.

The electroretinogram was normal in the early stages of the disease, but in the later stages first the negative wave could not be detected and finally the *b*-wave was lost.

In histological preparations the central retina was found to be degenerate, the pigment epithelium dystrophic, and the choroid somewhat thinned.

Material and Methods

The methods and terminology have been described previously (Parry, 1953 a, b, c). Fifteen cases have been under observation, details of which are given in the Table (overleaf).

Ten were examined at autopsy. Electroretinography was carried out in four cases by the team (Parry, Tansley, and Thomson, 1953). Of the fifteen dogs, eleven were referred to us by their owners on account of defective vision, nine being trained gundogs and two house pets. The remaining four (Cases 1–4) were animals being kept in our research kennels in connection with our studies of hereditary generalized retinal atrophy (Parry, 1953b).

Results

(1) Changes in the Eye.—The clinical and pathological data in these cases showed a striking sequence of increasing severity, and it is convenient to describe them as the three stages of a single syndrome, affecting both eyes symmetrically, each stage being sub-divided into an early phase (*a*) and a late phase (*b*).

Stage 1.—Day and night vision and the electroretinogram were normal, but small foci of hypertrophic pigment epithelial cells appeared, which in Stage 1*a* could only be detected in microscopic preparations. During Stage 1*b* the atrophy of the retina commenced and

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TABLE

DETAILS OF DOGS AFFECTED WITH CENTRAL RETINAL

Case No.	Breed	Sex	Age when Disease First Noted (yrs)	Clinical Examination		Electroretinogram
				Age (yrs)	Stage of Disease	
1	Border Collie (DO 49)	M	—	1½	0	—
2	Border Collie (DO 48)	F	—	2	0	—
3	Red Irish Setter (DH 18)	F	1½	1½	1 *b*	Normal then slow loss of negative wave
4	Border Collie (DO 51)	M	3	3	1 *b*	Normal
5	Black Labrador	F	2	3	2 *a*	—
6	Black Labrador	M	1	1½	2 *a*	—
7	Yellow Labrador	M	3	4	2 *a*	—
8	Springer Spaniel	F	2½	3	2 *b*	—
9	Black Labrador	F	2½	3	2 *b*	—
10	Golden Retriever	F	5	9	2 *b*	*b*-wave and negative wave of low voltage
11	Black Labrador	M	5	6	2 *b*	—
12	Black Labrador (DO 76)	M	1½	2	2 *b*	*b*-wave and small wave both gradually lost
13	Black Labrador	M	7	8	3 *b*	—
14	Collie × Irish Water Spaniel	M	8	12	3 *b*	—
15	Black Labrador	M	2	8	2 *b*	—

foci of hypertrophic pigment epithelial cells were visible on ophthalmoscopic examination.

Stage 2.—The dog showed signs of a central scotoma with good peripheral vision. The electroretinogram could still be detected but the negative wave was of low voltage and was gradually lost, followed by loss of the *b*-wave. The pigment foci remained. The central retina became completely sclerosed while the peripheral retina remained normal.

Stage 3.—Peripheral vision was lost. An electroretinogram was not detectable. The peripheral fundus underwent atrophy (Stage 3*a*) which progressed to complete sclerosis (Stage 3*b*).

The terms atrophy and sclerosis are used to denote the two stages: the first in which the layer organization of the retina persisted, and the second in which it was lost in an unorganized glial matrix.

ATROPHY WITH PIGMENT CELL DYSTROPHY

Pathological Examination			Stage of Disease	Pertinent Medical History	Disease Type
Age (yrs)	Central Retina*	Peripheral Retina*			
1½	PE hypertrophy Atrophy	Normal	1 *a*	Virus hepatitis at 1½ yrs	A
2	PE hypertrophy Atrophy	Normal	1 *a*	Virus hepatitis at 1½ yrs	A
2	Atrophy +	Normal	1 *b*	Para-distemper at 3 mths; inapparent virus hepatitis at 1 yr	B
3	Sclerosis +	Normal	2 *a*	Virus hepatitis at 1½ yrs	A
—	—	—	2 *a*	—	A
—	—	—	—	None	A
4	Sclerosis +	Normal	2 *b*	Jaundice at 1 yr	A
—	—	—	—	Severe para-distemper at 2 yrs	B
—	—	—	—	None	A
9	Sclerosis ++	Normal	2 *b*	None	A
8	Sclerosis +	Atrophy ++	2 *b*	None	A
3	Sclerosis +	Atrophy +	3 *a*	None	A
8	Sclerosis ++	Sclerosis +	3 *b*	Convulsions and mental confusion at 10 mths	A
12	Sclerosis ++	Sclerosis +	3 *b*	None	B
—	—	—	—	None	A

*moderate + severe ++

STAGE 1

Clinical Data: Four cases were observed in this stage. The earliest sign of the disease will only be detected during frequent routine ophthalmoscopic examinations. The first sign of the disease, before any visual defect was noted, was the appearance of foci of brown pigment over the tapetal fundus. These foci were irregular in outline and 0·05–0·1 mm. in diameter. They appeared 0·5–2·0 mm. apart and were not related to the retinal blood vessels. The texture of the fundus, the stellulae of Winslow, and the retinal blood vessels were normal, although the granularity of the fundus was somewhat reduced; the papilla was rather pale but otherwise normal. The average pupil size tended to be rather larger than normal, *i.e.* 6–8/14 mm. Day and night vision were normal. The size and tension of the eyeballs were normal, as were the other ocular structures.

Electroretinography.—The electroretinogram was normal in one dog (Case 4), but in another animal, Case 3, in which it was recorded six times between the ages of 1 and 2 years while the pigment foci were developing, there was a gradual reduction of the slow negative component of the electroretinogram in both eyes, although there was no detectable defect of day or night vision.

Morbid Anatomy.—Three cases were examined at autopsy; no macroscopic abnormality of the optic nerves or brain was found.

Histology.—In the earliest phase, (Stage 1*a*; Cases 1 and 2) the retina was virtually normal, the only lesion being a moderate thickening of the cells of the pigment epithelium to about 7–8 μ in small foci up to 20 μ in diameter (Case 1). This hypertrophy spread and involved the epithelium over most of the tapetal fundus in Case 2, which was 6 months older at death than her litter-brother Case 1; at the same time a definite increase of glial fibres just beneath the internal limiting membrane was apparent and the ganglion cells were rather less numerous than normal near the papilla. The remaining layers of the retina appeared normal. The choroid was

FIG. 1.—Section through retina of 2-yr-old Red Irish Setter dog (Case 3) at Stage 1*b* of central degeneration, showing ventral edge of tapetal fundus near papilla. Note giant cell in pigment epithelium. There is gliosis of the optic nerve fibre layer. The large retinal blood vessel, the chorio-capillaris, and the trans-tapetal capillary on the left are all normal. Intravital fixation with Kolmer's cold-blooded fixative. Mallory's phosphotungstic acid haematoxylin. ×330.

The following code for labelling the retinal structures applies to all the figures:

Sc. Sclera
Ch. Choroid
Tap. Tapetum
C.C. Chorio-capillaris
Ret. Retina
1. Pigment epithelium
2. Rod and cone layer
3. External limiting membrane
4. Outer nuclear layer
5. Outer fibre layer
6. Inner nuclear layer
7. Inner fibre layer
8. Ganglion cell layer
9. Optic nerve fibres
10. Internal limiting membrane

slightly less thick than usual and its blood vessels less prominent, but they were otherwise normal.

In the late phase (Stage 1*b*, Case 3) signs of an early atrophy of the retina occurred symmetrically over the whole of the tapetal fundus and the immediately adjacent dorsal non-tapetal fundus. The peripheral fundus remained normal apart from some increase of glial fibres, but in the central fundus the changes involved the pigment epithelium, the rods and cones and their nuclei, and the ganglion cells and nerve fibre layer. The inner nuclear and adjoining fibre layers were but little affected. The abnormalities in the pigment epithelium ranged from an occasional large hypertrophic cell 10 μ long and 15 μ wide (Fig. 1), through bizarre-shaped pigment cells heavily loaded with light-brown refractile pigment granules (Fig. 2) staining a deep blue with the azan technique, to multicellular " nests " of pigment cells up to 100μ long and 40–50μ wide (Fig. 3, overleaf), the cells of which were less heavily loaded with similar pigment granules. The rods and cones were reduced very considerably immediately adjacent to the enlarged pigment cells and the " nests " (Figs 1, 2, and 3), but elsewhere they were little affected although the outer limbs appeared less robust than usual. Over the mid-tapetal fundus there was a general reduction in the thickness of the rods and cones and of the outer nuclear layer due to loss of rod nuclei (Fig. 2), and in some foci adjacent to the giant pigment cell " nests " the rods and their nuclei were completely absent. The ganglion cells were somewhat less numerous than normal, and most of the remaining giant ganglion cells showed evidence of degenerative changes in the loss of definition of the cell components. The optic nerve fibres were reduced, particularly near the papilla, and the papilla itself was vacuolated and shrunken, while the optic nerve central to the lamina cribrosa showed less marked degenerative changes. The

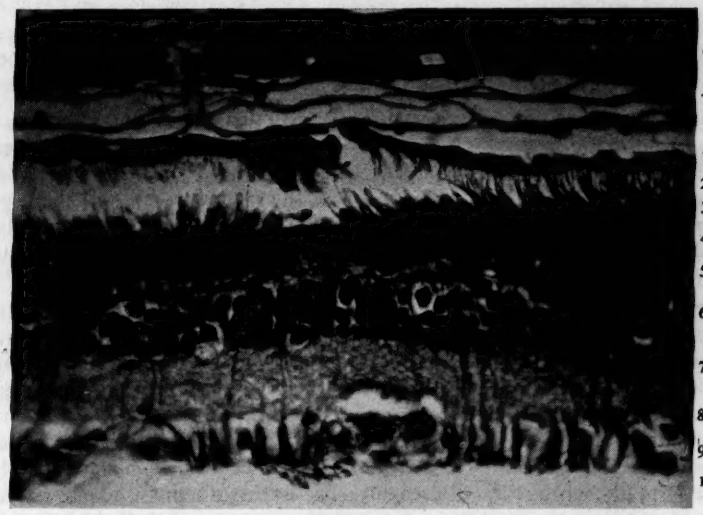

FIG. 2.—Same preparation as Fig. 1, mid-tapetal fundus. Note occasional bizarre-shaped pigment epithelial cells, and adjacent disappearance of rods and cones and outer nuclear layer. The remainder of the outer nuclear layer is about half the normal thickness. The inner nuclear and adjoining fibre layers are normal. ×330.

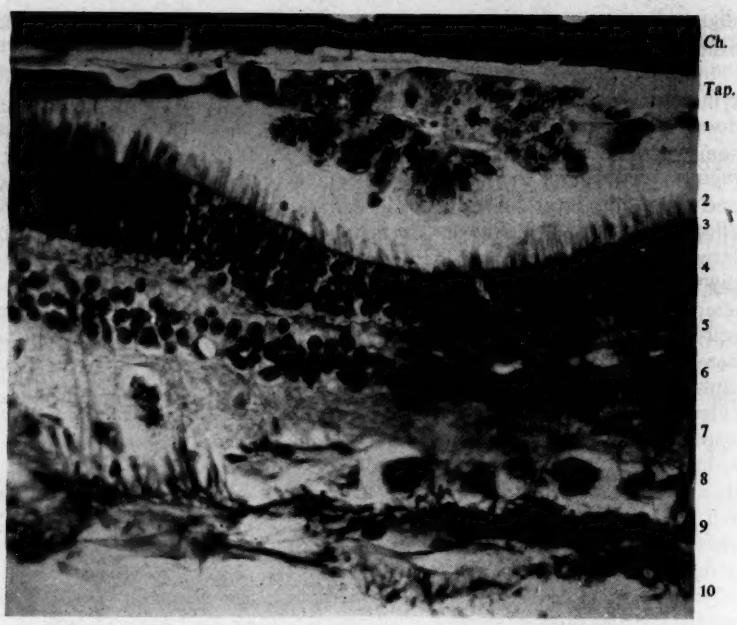

FIG. 3.—Same preparation as Figs 1 and 2, mid-tapetal fundus near papilla. Note hypertrophied pigment epithelium with giant multicellular " nest ", adjoining which the rods and cones are much reduced. The ganglion cells are degenerate and there is gliosis of the optic nerve fibre layer. ×270.

terminations of Müller's fibres adjacent to the internal limiting membrane were much increased in number and thickness, and their nuclei stained very deeply.

Case 3 showed certain features not observed in the others. The choroid was not reduced in width, being about 150 μ wide, but the tapetum was narrower than usual and the sides of the cells less regularly arranged (Fig. 2). The centres of many of the multicellular " nests " showed hyaline changes, and there was, in the mid-non-tapetal fundus, about 2 mm. from the papilla, a focus of advanced sclerosis in which an old thrombosed blood vessel was present. Elsewhere the blood vessels of the choroid and retina were normal.

STAGE 2

Clinical Data.—Nine cases were examined at this stage. Vision was obviously abnormal. A common observation with gundogs was that they failed to " mark " a falling bird, and would " over-run " their quarry in retrieving. The dogs could see large objects and recognize their owner at a distance, but had difficulty in seeing near objects, especially if they were small and placed on the ground, *i.e.* the signs one might expect to observe in a dog with a central scotoma. These defects were not apparently more marked at night. The average pupil size was increased to 8–10/14 mm. and varied considerably with the direction of the light beam; the eye preservation reflex was present but sluggish; the pupillary light reactions were sluggish; the lenses and media were clear and the other ocular structures normal.

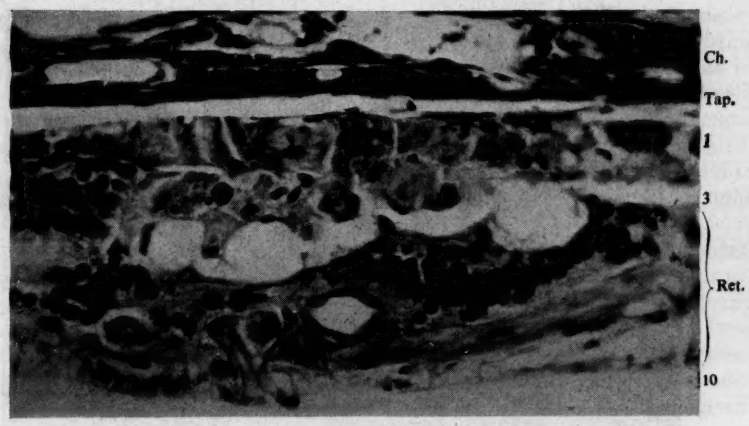

FIG. 4.—Section through retina of 3-yr-old Border Collie dog (Case 4) at Stage 2*a* of central degeneration; mid-tapetal fundus near papilla. Retina sclerosed. Note giant multicellular " nest " separated in centre from sclerosed retina by cavities situated where rods and cones should be. The choroidal and retinal blood vessels appear normal. Intravital fixation with Kolmer's cold-blooded fluid. Mallory's phosphotungstic acid haematoxylin. ×330.

The tapetal fundus showed the foci of brown granular pigmentation distributed irregularly, and about 0·1–0·2 mm. in diameter, the texture was slightly crystalline, but the stellulae of Winslow remained. The reflection was increased slightly. The blood vessels of the tapetal fundus were reduced in number; those of the non-tapetal fundus were still normal in distribution but had lost their " silver wiring" reflection. The papilla was pale but its primary blood vessels were normal.

Electroretinography.—This was carried out in three cases. The electroretinogram was normal at the beginning of Stage 2 (Case 4), but later the voltage of the negative wave was reduced (Case 10). Case 12 was tested on three occasions in 6 months during which it became completely blind; on the first two occasions a small *b*-wave was present without a negative wave, and on the last occasion the *b*-wave was also missing.

Morbid Anatomy.—Four cases were examined. No significant lesions were noted.

Histology.—The principal features were the continuing degeneration of the central area of the retina until it was completely sclerosed (Fig. 4), while the peripheral fundus remained remarkably normal (Fig. 6), the junction between the two areas being sharply defined (Fig. 5). The retinal blood vessels remained as numerous as in a normal animal.

The central part of the retina, *i.e.* the whole of the tapetal fundus and the ventral non-tapetal fundus at least half way to the *ora serrata*, showed loss of the layer organization (Fig. 4) with irregular masses of nuclei, the remnants of the two nuclear layers. Occasional ganglion cells remained. There were no rods or cones. The blood vessels were normal and were quite as numerous as in a normal retina. The pigment epithelium had disappeared in many places, while in others the multi-

FIG. 5.—Same preparation as Fig. 4, junction between sclerosed and normal retina, dorsal junctional zone. Note gradual return of normal retinal layers and pigment epithelium from sclerosed central fundus on left to more normal peripheral fundus on right. With the appearance of less dystrophic pigment epithelium the rods and cones and the outer nuclear layer reappear. The pigment epithelium is still hypertrophied without its normal pigmentation on the right. Ganglion cells are scanty. The thickness of the choroid is reduced. ×330.

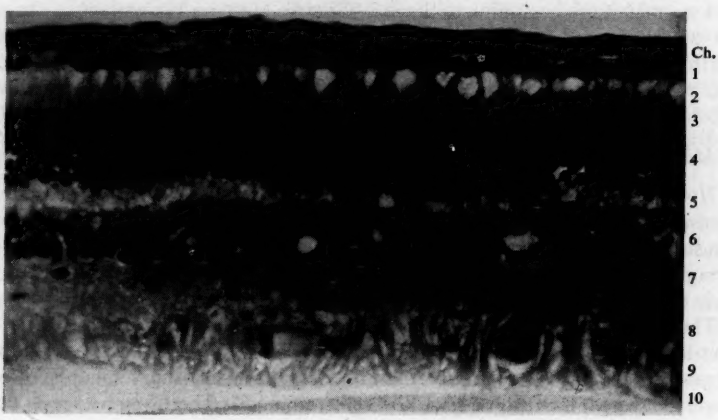

FIG. 6.—Same preparation as Figs 4 and 5; dorsal peripheral non-tapetal fundus. Retina essentially normal. Note normal lanceolate pigment granules in pigment epithelium, and retinal capillaries in inner nuclear and ganglion cell layers. ×330.

cellular " nests " had enlarged into irregular masses of cells up to 200 μ in diameter, lightly loaded with pigment granules; in yet other portions the pigment epithelial cells were swollen and rounded, 12–15 μ in diameter and with rounded instead of the normal square ends where attached to adjoining pigment cells, and some cells were seen in mitosis. In occasional sites similar cells formed a " cuff " around retinal blood vessels away from the pigment epithelial layer, and more rarely individual pigment cells were seen in the sclerosed retina. The optic papilla was reduced in size and much vacuolated with loss of nerve fibres. The orbital portion of the optic nerve was much less severely affected.

The junction of the central sclerosed part of the retina and the normal peripheral part formed a well-marked ring about 0·5 mm. wide (Fig. 5), in which the normal layers of the retina were present but the pigment epithelium and rods and cones were abnormal. At the central margin the pigment epithelium assumed its normal layer form (Fig. 5), but the cells were still hypertrophic and without normal pigment granules; the rods and cones were absent or reduced to stubby inner limbs only, and the external limiting membrane was no longer firmly adjacent to the pigment epithelium (centre of Fig. 5).

Towards the peripheral margin of the ring the cells of the pigment epithelium were normal in size, and eventually normal lanceolate pigment granules appeared (Fig. 6); coincident with these changes the rods and cones became normal.

The peripheral part of the retina, *i.e.* the dorsal and ventral peripheral zones and the peripheral part of the mid-tapetal zone, was essentially normal in general morphology (Fig. 6), although there was some gliosis of the nerve fibre layer. The pigment epithelium was normal in size and in the nature and distribution of its pigment granules. Retinal blood vessels were numerous. As these animals had some vision and electroretinograms were recorded from two of them, the functioning of this portion of the retina must have been to a great extent normal.

Blessig-Henlé cavities were present in both eyes of two cases and extended up to 1 mm. from the ora serrata, *i.e.* twice as far as normally; away from the ora serrata the cavities involved the inner nuclear layer only.

STAGE 3

Clinical Data.—Four cases were examined. This stage was characterized by the loss of peripheral vision and the development of complete blindness. The pupils were dilated and did not respond to light, the average pupil size was 10/15 mm., and the eye preservation reflex was absent. The lenses were clear and no abnormalities of the iris were noted. The tapetal reflection was increased. The fundus was difficult to bring into focus owing to refractive distortion, apparently in the vitreous adjacent to the retina, and the fundus was seen best with a −10 or −15 lens; it showed little change apart from swirling and apparent loss of blood vessels, many of which could be seen buried within the retina. The focal pigment accumulations had disappeared in the advanced cases. The optic papilla was remarkably white, although blood vessels were present.

Electroretinography.—No electroretinogram could be detected in the one animal in which a recording was attempted.

Morbid Anatomy.—No significant lesions were noted in the two cases examined.

Histology.—This stage was similar to the last except that the sclerosis of the central retina was more advanced and the peripheral portion with layer organization

was still further reduced. The central portion of the retina was reduced to a sclerosed ribbon 10–40 μ wide. The pigment epithelium was absent except for occasional multicellular " nests ", which were disintegrating. Occasional large round cells, some with pigment and some without, occurred throughout the sclerosed retina unrelated to the remaining blood vessels.

The degeneration of the retina had extended further towards the ora serrata, where the extreme peripheral 1–1·5 mm. of retina alone retained the layer organization, this portion being slightly wider ventrally. One case showed marked Blessig-Henlé cavities in one eye, chiefly in the inner nuclear layer.

(2) Rate of Development of the Disease.—As the earliest clinical signs of the disease can only be detected by ophthalmoscopic examination, and the lesion of the central fundus produces such inconspicuous disturbance of vision, the development of Stage 1 is often overlooked and data relating to it are scanty. Cases 3 and 4, in which an *ante-mortem* diagnosis was made at this stage, were 1½ and 3 years old respectively. Nine cases were in the second stage, in which impaired vision is noticeable; this stage either persisted for several years, during which the disease was apparently stationary (Cases 7, 10, 11, and 15), or progressed to Stage 3 with complete blindness and the loss of the electroretinogram in about 12 months (Case 12). The presence of some vision after 4 years of known defective vision in Case 10 (which still had an electroretinogram) and after 6 years in Case 15 suggests that the peripheral zone of the retina can be affected extremely slowly by the degenerative process.

(3) Associated Defects.—There were no other ocular abnormalities, except in Case 15, which had small floating opacities in the vitreous humour of the right eye. There have been no other clinical defects of the nervous system. The general health and development of the dogs were excellent. The gundogs in particular were exceptionally intelligent and several had done well in field trial competitions.

(4) Occurrence of the Disease.—The fifteen cases fall into two groups: Type A, with a marked breed or family incidence, in which the electroretinogram is normal until the disease is far advanced, and Type B, those without evidence of breed or family incidence, in which changes in the electroretinogram may appear at an earlier stage.

Type A.—There were twelve cases: three Border Collies and nine Retrievers.

The Border Collies (Cases 1, 2, and 4) had been kennelled together at the Research Station with normal dogs used as controls in other studies (Parry, 1953b). They were the survivors of a litter of five, the progeny of a son × mother test-mating, sent to us at weaning. One pup died of acute leptospirosis at 6 months old and the other died suddenly 3 months after apparent recovery from severe virus hepatitis (Parry, 1950). They had never, as far as is known, been in contact with viruses of the distemper-complex. The mother was blind with a retinal atrophy of uncertain aetiology, which had been first noticed when she was about 4 years old; she was examined at 8 years old when the clinical signs were those of advanced generalized retinal atrophy. No pathological examination was possible. Her son was not examined, but was said to have normal vision.

Of the nine Retrievers, eight were Labradors; six of the nine were males and three females (Table). There was no significant medical history in seven cases; one had convulsions and mental confusion in adolescence which may have been associated

with distemper-complex infection, and another had had jaundice of unknown aetiology.

Of the eight Labradors, pedigrees were available for Cases 7, 11, 12, 13, and 15, but no details of litter-mates could be obtained. None of these animals was closely related; however, the paternal grandsire of Case 13 was a maternal great-great-grandsire of Case 15, and a paternal great-great-great-grandsire was common to Cases 7 and 12. Case 11 had no ancestors to the fourth generation in common with the others. A full pedigree was not available for Case 9, but its father had gone blind at 2 years old, and of its three litter-mates, a brother was alive and said to have normal vision, while two sisters had died of para-distemper when 3 years old without abnormal vision being noted. A litter of four pups by Case 9 were alive and the eyes of two examined at 1 year old were normal.

Type B (Cases 3, 8, and 14).—These three cases form a miscellaneous group of one male and two females, of which only Case 3 provided histological data of real value, Case 14 being at a very advanced stage of the disease when examined. Cases 3 and 8 were known to have had para-distemper: in Case 8 the owner associated the onset of defective vision with a severe attack accompanied by other neurological signs which later disappeared. Case 3, a Red Irish Setter, was the progeny of a test-mating for the hereditary generalized atrophy (Parry, 1953b), being the only survivor of three litter-mates received at 4 months old while incubating para-distemper; the two litter-mates died from acute para-distemper encephalopathy, but this dog had only a mild febrile illness without clinical signs of involvement of the nervous system.

Discussion

The data from these fifteen cases of central progressive retinal atrophy, of which ten were examined pathologically, form a well-defined syndrome of bilateral central retinal degeneration with pigment epithelial dystrophy. The syndrome is quite distinct from those reported previously in this series of papers.

The first stage of the disease usually develops during early adult life, although in some no sign of the disease was noted until after middle age. The onset is indefinite on account of the slow development of the central scotoma. The earliest stage of the disease will often go unrecognized unless routine ophthalmoscopic examinations are being made. Peripheral vision, both by day and night, remains normal until the third stage of the disease, and until then the peripheral portion of the retina is probably fully functional since the electroretinogram is normal. The degeneration affects the retina of the central fundus, including the whole of the tapetal fundus as far as the outer part of the mid-ventral zone, *i.e.* about half-way to the ora serrata. The area of affected fundus is rather more extensive in the dorsal than the ventral quadrants.

The pigment epithelium is the first layer of the neuro-epithelium to show any abnormality. The typical foci of pigment epithelial cells can only be seen with the ophthalmoscope over the tapetal fundus, but histological preparations show that the foci also occur over the non-tapetal fundus, where their presence is masked in life by the underlying choroidal pigment.

Only when the pigment epithelium is definitely dystrophic with hypertrophic cells and multicellular " nests " do the rods and cones begin to show degenerative changes. These changes are particularly marked near the multicellular " nests ", but there is a general loss of first-order neurones over the whole of the central fundus, until the rods and cones disappear and the outer nuclear layer is reduced to a single layer of cone nuclei. The inner nuclear layer remains normal until a later stage and it forms the bulk of the residual nuclei which finally fuse to form a single irregular nuclear layer. At an early stage of the degeneration, before there is any appreciable loss of first-order neurones, the optic nerve fibres of the papilla and immediate peripapillary zone show degeneration and vacuolation, which is no doubt responsible for the abnormal pallor of the papilla noted in life. About the same time the glial network immediately adjacent to the internal limiting membrane becomes prominent through the proliferation of Müller's fibres, the nuclei of which stain abnormally prominently. There is a modest loss of large ganglion cells, particularly near the papilla, but some large ganglion cells remain even when the retina is sclerosed.

The dystrophy of the pigment epithelium shows three features of special interest: general hypertrophy with abnormal pigment formation, individual giant cells, and multicellular " nests ". These are probably three phases of the same reaction to an abnormal environment, for the hypertrophic cells have been observed in metaphase, and from such dividing cells the multicellular " nests " could readily arise. These features have not been observed in normal eyes, but a modest generalized regular hypertrophy and a massive irregular focal hypertrophy occur in distemper retinopathy (Parry, 1954). However, in distemper retinopathies, the pigment cells maintain a regular layer arrangement, while in central atrophy the cells tend to have convex ends, become rounded, and form small groups, and some of them may break away from the layer as loose cells. The multicellular " nests " are presumably a more advanced stage of cell proliferation; they do not occur in close relation to blood vessels, although occasionally a focus was seen immediately beneath a large retinal artery.

Proliferation of the pigment epithelium has been reported in amphibia following experimental removal of the retina (Stone, 1950), and it occurs in some human cases of nephritic retinitis (Koyanagi, 1934; Duke-Elder, 1940a) and pseudo-retinitis pigmentosa (Cogan, 1950). Koyanagi shows a multicellular " nest " in Fig. 12 of his paper, which is very similar to those seen in these dogs. The masses of heavily pigmented cells illustrated by Cogan in Figs 24–29 of his paper are less similar, but it is of interest that there is evidence of an old inflammatory reaction with choroidal damage in each of his three cases. In these instances of dystrophy of the pigment epithelium in man there are grounds for believing that the circulation through the adjoining choroid has been inadequate, and it seems probable that these types of pigment dystrophy may be related to a pre-existing insufficiency of the choroid and its circulation due to inflammation or other causes. On

the other hand, Keyes and Goldblatt (1938) observed atrophy of the choroid in dogs with experimental malignant hypertension, in which severe damage to the walls of the blood vessels of the uveal and retinal systems occurred; their report contains no special mention of pigment epithelial dystrophy, although they observed iron-containing pigment in old retinal scars following extensive haemorrhages into the retina.

The occurrence of such extensive pigment dystrophy invites consideration of any possible relationship between the dog syndrome and human diseases of the retinitis pigmentosa group. Sorsby (1940), discussing abiotrophies of the retina and choroid, mentions two types of central retinal abiotrophy: macular dystrophies and angeoid streaks. Although there is a not dissimilar defect of vision in the former, neither seems at all similar to the dog disease, since the dog does not have a macula and the atrophy is not confined to the area centralis, nor have fundus changes resembling those seen in man been observed in the dog. Similarly, in the classification of the primary chorio-retinal aberrations with night blindness occurring in man (Leinfelder, 1950), there is no category into which the canine central atrophy appears to fit.

However, the syndrome described by Stock (1908, 1936) provides a closer resemblance. He reported on three human cases of retinal degeneration with pigment dystrophy, first affecting the central fundus and then spreading slowly outwards towards the periphery. Night blindness did not occur until day vision was nearly lost, but other serious defects of the central nervous system indicative of widespread damage to the brain developed, a complication absent in the dog. The aetiology of Stock's syndrome is uncertain, and any close comparison with the dog disease must remain speculative in the absence of detailed histological data.

The first cases of the dog disease suggested that we might be dealing with a form of central angiospastic retinopathy (Gifford and Marquardt, 1939; Duke-Elder, 1940b), or of the central serosal retinitis common in Japan (Asayama, 1892; Masuda, 1918; Oguchi, 1922; Kitahara, 1936), which Ko (1935) has suggested might be due to some pathological photosensitization of the central retina. However, in these syndromes, oedema of the macula occurs and recovery without permanent impairment of vision is usual, although recurrences often occur in the angiospastic retinopathy; these features have not been observed in the dog syndrome. We have also failed to observe signs of angiospasm in life, nor have microscopic abnormalities of the remaining choroidal and retinal blood vessels been seen constantly. Similarly, any close relationship to the senile macular chorio-retinal degeneration of Haab (Duke-Elder, 1940c) seems unlikely, as the chorio-capillaris is spared in the dog disease and irregular sclerotic changes in the choroidal blood vessels have not been observed.

In short, we have failed to find a description of a human syndrome which resembles closely this central retinal atrophy of the dog, although it has similarities to some forms of retinitis pigmentosa.

Before discussing the aetiology of the dog syndrome, one should consider possible reasons for the central distribution of the degeneration and its sequence within the retina, which are, as far as we know at present, quite characteristic. The main features could be explained by postulating an inadequate circulation through the posterior portion of the choroid, thereby affecting the circulation to the chorio-capillaris of the central fundus and the outer layers of the overlying neuro-epithelium, whilst leaving intact the inner layers of the retina supplied by the central retinal artery. Such a disturbance would also explain the early degeneration of the papilla and peripapillary optic nerve fibres, a region supplied by the secondary cilio-retinal arteries arising from the choroidal circulation near the optic nerve head and probably receiving very little blood from the central retinal system.

There is some support for such an hypothesis from human and experimental ophthalmology. A similar distribution and type of degeneration has been reported in one human eye after the severing of the central retinal and posterior ciliary arteries (Komoto, 1915). In this eye 12 days after operation the whole of the central, *i.e.* posterior, fundus was sclerosed, while the extreme peripheral retina was spared and was essentially normal, although there may have been some loss of third-order neurones. The experimental severing of the posterior ciliary arteries of rabbits (Nicholls, 1938) produced a sequence of degeneration similar to that seen in the dog disease, but the degeneration was confined principally to the equator, although there was oedema of the central fundus. Nicholls found that the extent of the degeneration varied very much with the extent of the surgical interference, so that about two-thirds of the posterior ciliary arteries had to be severed to get an appreciable lesion, and that in producing this there was inevitably considerable damage to the ciliary nerves. It may well be that a more complete interruption of the blood supply through all the short posterior ciliary arteries would have produced a severe degeneration of the whole of the central fundus. The peripheral fundus in his rabbits was spared, as the anterior ciliary circulation was unaffected.

Sparing of the peripheral retina is also seen after occlusion of the central retinal artery in man (Hancock, 1908; Coverdale, 1929; Duke-Elder, 1940d), which suggests that the inner layers of the peripheral zone of the retina receive their blood supply from the choroidal rather than from the retinal system.

In central retinal atrophy in the dog, all the retinal layers of the posterior part of the eyeball are degenerate by the end of the first stage, *i.e.* the inner layers supplied by the central retinal system are not spared, although they are affected less early outside the peripapillary fundus. The choroidal circulation in this posterior region of the eyeball is probably supplied by the short posterior ciliary arteries (Nicolas, 1925a; Sisson and Grossman, 1938), although it is uncertain whether the branches of the short posterior ciliary arteries anastomose with those of the anterior ciliary arteries in the dog as they do in man (Nicholls, 1938), or whether the terminal branches of both anterior and short posterior ciliary arteries are end-arteries at the equator

as in the rabbit (Nicholls, 1938). The short posterior ciliary arteries probably arise direct from the ciliary artery (Nicolas, 1925a), while the anterior ciliaries arise from the artery to the extrinsic ocular muscles (Nicolas, 1925b), which is a branch of the external ophthalmic artery arising independently of the ciliary artery some distance central to the junction of the latter with the internal ophthalmic artery from the circle of Willis (Daniel and others, 1953).

The involvement of the inner layers of the retina does not necessarily imply interference with the blood supply of the central retinal system, as a similar degeneration follows degeneration of the first-order neurones, *e.g.* as in hereditary generalized atrophy. However, if the central retinal artery does arise from the short posterior ciliaries close to the eyeball (Wolff and Davies, 1931), and not from the external ophthalmic artery (Nicolas, 1925a; Sisson and Grossman, 1938), then disturbances in the posterior choroidal circulation may occur also in the central retinal system.

Thus it is possible to explain the principal features of the central atrophy on the hypothesis of an inadequate blood supply through the choroidal circulation from the short posterior ciliary arteries, followed by slow failure of the supply to the anterior parts of the choroid from the anterior ciliary arteries. A cardinal difficulty in accepting this explanation is that we have no satisfactory morphological evidence to support it, for, although the choroid may have been thinned slightly, there were no constant changes in the blood vessel walls and no signs of choroiditis, while the retinal blood vessels appeared to be, if anything, more numerous than usual. It is possible that any disturbance of the blood supply, whether due to anatomical or to physiological causes, may have been located in the orbit central to the eyeball, and may, therefore, have escaped attention. The use of our material for general cytological study precluded adequate study of these circulatory problems, the significance of which only came to light as a result of the cytological study.

These considerations, taken in conjunction with the data on the occurrence of the atrophy, suggest that the Type A cases are most probably due to a spontaneous abiotrophy (Treacher Collins, 1919). The breed and family incidence point to a genetic basis, although the evidence is as yet insufficient to establish the hereditary origin of the syndrome, let alone indicate its mode of inheritance beyond showing that it cannot be due to a simple Mendelian dominant gene or be completely sex-linked. The data from the Border Collie litter would fit inheritance by a simple Mendelian recessive gene. With regard to the three cases of Type B, the data is insufficient to exclude environmental factors such as distemper-complex infection, and, until more information is available, it seems wiser not to include them with the Retriever and Border Collie cases in the " possibly hereditary " category.

Summary

(1) A series of fifteen cases of progressive degeneration of the central portions of the retina with pigment epithelial dystrophy is described; ten cases were examined pathologically.

(2) Affected dogs develop a central scotoma by early or middle adult life while retaining normal peripheral vision by day and night, often for years.

(3) The retinal degeneration begins over the tapetal and dorsal non-tapetal fundus; hypertrophy of the pigment epithelium is followed by atrophy of the rods and cones and the outer nuclear layer, and sclerosis of the central retina.

(4) Multicellular " nests " of pigment epithelial cells occur; they may be seen in the tapetal fundus with the ophthalmoscope.

(5) The electroretinogram remains normal until the later stages of the disease, when first the negative wave and then the *b*-wave are lost.

(6) Two types of the syndrome are recognized: Type A, familial, in Retrievers and Border Collies, possibly due to an inherited abiotrophy; Type B, sporadic, of uncertain aetiology.

(7) The pathogenesis of the degeneration and the possible role of disturbances of the blood supply in its causation are discussed. The relationship of the disease to human retinitis pigmentosa is considered.

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TOPICAL CORTISONE IN THE TREATMENT OF SYPHILITIC INTERSTITIAL KERATITIS*

PRELIMINARY REPORT OF 20 CASES (26 EYES)

BY

GORDON O. HORNE

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THE majority of the reports which have been published on the treatment of syphilitic interstitial keratitis with topical cortisone have been concerned only with the more or less immediate effects of the hormone, and very few cases observed for more than about a year have been included. The reports have been conflicting, some authors obtaining excellent results, and others mediocre or poor results. Some authors maintain that cortisone may be contraindicated in interstitial keratitis, and some have even discarded it entirely.

On theoretical grounds, the correct use of cortisone would be expected to produce excellent results in interstitial keratitis, provided that treatment is started early enough. However, although cortisone is freely available for this purpose, there still appears to be some reluctance to use it, and when it is used the dosage is often inadequate. It has therefore been considered desirable to describe here briefly a series of cases which, it is hoped, will help to dispel any doubts about the value of cortisone in this condition and to establish it as an imperative method of treatment.

The three principal criteria for assessing the effectiveness of cortisone in interstitial keratitis are:

(1) its immediate effect on the inflammatory condition and the associated distressing symptoms;

(2) the duration of individual attacks and the incidence of relapses;

(3) the final visual acuity.

In this report only brief reference will be made to the first two; more consideration will be given to what is probably the most important criterion (and the one easiest to assess)—the final visual acuity. A further paper is in preparation, in which the rationale of the use of cortisone in interstitial keratitis will be discussed, the relevant literature reviewed, full clinical data of the series of cases described here recorded, and conclusions drawn from the information available as to the best way of using cortisone in this condition.

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TABLE

VISUAL ACUITY AFTER TREATMENT OF INTERSTITIAL KERATITIS:

Adapted from:	Author	†Klauder and Vandoren	Klauder	
	Date	1941	1947	
No. of Patients		Not stated	54	59
No. of Eyes		63	96	97
Treatment Schedule		Arsenic, bismuth, artificial fever	Arsenic, bismuth, artificial fever	Penicillin, with or without fever and/or chemotherapy
Time of Assessment		At least one yr after starting treatment	About 2½–10 yrs after treatment	One yr or less after penicillin treatment
Final Visual Acuity (corrected) Percentage Distribution	6/6 or Better 6/9, 6/12	31·7 23·8 } 55·5	14·0 47·5 } 61·5	20·5 35·0 } 55·5
	6/15–6/30	31·7	27·5	34·0
	Less than 6/30	12·7	11·0	10·5

†Visual acuity not "corrected" in every case.

Clinical Material

Between December, 1950, and January, 1954, twenty patients attending the Department of Venereal Diseases, General Infirmary, Leeds, were treated with topical cortisone for the first attack of syphilitic interstitial keratitis. Half of them had had an attack previously in one eye, and only the second eye to become affected was treated with cortisone; 26 eyes, with a wide range of severity of involvement, were treated. In nearly every patient drops of a cortisone acetate suspension (5 mg./ml.) were used exclusively; the majority were admitted to hospital for at least part of the time they were receiving drops; all of them also received systemic antisyphilitic treatment (penicillin, with or without bismuth).

All of the patients were kept under periodic observation, and a special review, which included biomicroscopy, was made in March and April, 1954. The duration of observation after starting cortisone was as follows:

Months	6–11	12–23	24–35	36–39
No. of Eyes	4	6	12	4

Results

In nearly all the cases the immediate effect of cortisone was excellent; there was rapid relief of symptoms, suppression of inflammation, and restoration of normal vision. In some the improvement was slower, and the rate was influenced partly by the duration of the disease before treatment was started, but principally by the dosage of cortisone. There was no evidence to suggest

COMPARISON OF PRESENT SERIES WITH SERIES PREVIOUSLY REPORTED

Graham and others	Oksala			‡Present Investigation
1948	1952	1953		1954
"49 cases"	Not stated	24	11	19
	157	35	18	25
Arsenic and bismuth, some with fever	Arsenic and bismuth	Penicillin, with or without fever	Penicillin, fever, and topical cortisone	Penicillin, bismuth, and topical cortisone
Unqualified, but probably several years in most cases	Unqualified, but probably many years in most cases	Average 1½ yrs after treatment	Average 1 yr after treatment	6–39 months after starting cortisone (see text)
53	22·3, 31·8 } 54·1	60	100	36, 52 } 88
37	27·3	26	0	*12
10	18·5	14	0	0

‡One patient (one eye) omitted (see footnote in text).

*Three eyes: Visual acuity (Case 18) 6/24 and (Case 19) 6/18 both have corneal scarring; (Case 10) 6/18 cornea functionally normal, but healed chorioretinitis involving macula (see text).

that when adequate dosage was used attacks were prolonged; in fact, the results could be interpreted as indicating that adequate dosage might shorten attacks. The series is too small and the period of observation too short to draw conclusions about the relapse rate, but there was no evidence to suggest that this was greater than might have been expected if cortisone had not been used. Relapses were equally well controlled. So also was any accompanying iridocyclitis.

The visual acuity (corrected for refractive errors) at the time of the last review is summarized in the Table, which also presents data adapted from the literature suitable for comparison by this criterion. These represent the final visual acuity obtained by the best methods of treatment in use before cortisone was available. The Table also includes another cortisone-treated series. These data, though the most suitable that could be found for the purpose, are not strictly comparable (especially in view of the differing observation periods), but even so the Table clearly demonstrates the superiority of topical cortisone. In only three of the 25 eyes in the series reported here was the final visual acuity less than 6/12.* In one of these (V.A. 6/18), the cornea was functionally normal and the impaired vision was almost certainly

*One patient (one eye) has been omitted from the analysis. She has been blind in one eye for many years as a result of corneal scarring and chorioretinitis, but the cornea treated with cortisone appeared (34 months after treatment was started) to be functionally practically normal, and there was no evidence of other ocular disease. For some reason, not yet determined, the patient feigned blindness.

due to an old chorioretinitis involving the macula. In two others (V.A. 6/18 and 6/24), the impaired vision was probably due at least in part to corneal scarring; the management of these two cases had been in some respects unsatisfactory, since corneal opacities were allowed to develop during a period when the patients were not under regular supervision, and when cortisone was either not used, or given in inadequate dosage.

In this series no contraindication to the use of cortisone was revealed.

Summary

In order to emphasize the great value of topical cortisone in the treatment of syphilitic interstitial keratitis, and to help to establish it as an imperative method of treatment in this condition, a series of twenty cases (26 eyes) so treated has been briefly reported. When adequate dosage of the hormone was used and the cases were well managed, excellent immediate and long-term results were always obtained; in the whole series, judged by the ultimate visual acuity (measured at periods ranging from 6 to 39 months after the start of treatment), the results were much superior to those reported to have been obtained by other methods of treatment. No contraindication to the use of cortisone was revealed. A more detailed report of the cases is to be published.

The author is indebted to Mr. G. W. Black, Mr. J. Foster, and Mr. J. Sherne for their collaboration in the treatment of these patients. They do not necessarily agree with the views of the author.

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INHIBITION OF SUGAR METABOLISM IN THE LENS*

BY

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OF all the theories advanced to explain the pathogenesis of cataract, the one which seems to have withstood the test of time most satisfactorily is that which ascribes the opacification to a defect in the carbohydrate metabolism of the lens. The most adequate experimental method of obtaining proof of such a theory is to block the sugar metabolism in the lens and observe the results.

This was undertaken by Nordmann and Dillschneider (1951) in their first series of experiments. Interrupting the sugar metabolism by glyceraldehyde, they observed the formation of opacification in the lens, associated with a fall in the production of lactic acid and in the accumulation of energy-rich compounds (adenosine triphosphate) (ATP). We have followed up these experiments using a series of inhibitors—mono-iodacetic acid, sodium fluoride, phloridzine, sodium malonate, and fluoro-acetic acid. This paper gives the results of these experiments, combined with those obtained by Nordmann and Dillschneider.

Methods

During each experiment we compared the two lenses of the same calf, maintained in a perfusion medium; the control lens was kept in a tyrode glucose medium (1 in 1,000), a solution comparable to the aqueous humour; the other lens was kept in the same solution with the addition of the inhibitor, without altering the osmotic pressure, the *p*H, or the *r*H of the solution (Figure). The medium, sterilized by tyndalization, was maintained at 37° C. throughout the experiments.

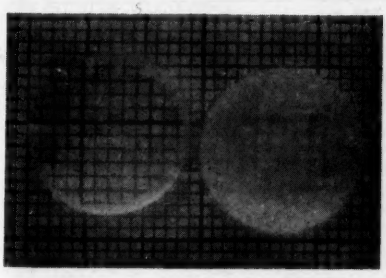

FIGURE.—*Cataract by arrest of the sugar metabolism of the lens.*—The photograph was taken after 24 hrs' perfusion; the lens on the left was in the control solution, that on the right in sodium fluoride (2/1,000). The difference in transparency between the two lenses is well shown. The experimental cataracts produced with the other inhibitors were strictly comparable.

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Chemical Methods.—The determination of lactic acid followed two methods:

(1) that of Lieb and Zacherl (1932), modified by Fromageot and Heltz, with the apparatus of Fuchs (1933);

(2) that of Barker and Summerson (1941).

ATP was estimated by the method of Lohmann (1928), modified by Cori. Micro-estimations of citric acid were prepared by the method of Weil-Malherbe and Bone (1949).

Results

(1) GLYCERALDEHYDE (0·4 to 1·5 g./l.)

(*a*) *Action on Transparency of Lens.*—With these quantities of glyceraldehyde, lenses maintained in the medium for more than a day clouded and turned a yellowish colour.

(*b*) *Action on Carbohydrate Metabolism of Lens.*—The results of each experiment are seen in Table I. In contrast with the control lens, a fall in the concentration of lactic acid and of ATP was observed in each lens in the medium containing glyceraldehyde. The quantity of lactic acid in the medium remaining after the perfusion of the cataractous lens was also less than that in the medium containing the control lens.

TABLE I

EFFECT OF GLYCERALDEHYDE ON CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Duration of Perfusion (days)	Quantity of Glyceraldehyde (g./l.)	Quantity of Lactic Acid (mg./100 g. fresh lens)	Quantity of Lactic Acid (mg./100 ml.) in Liquid in which Lens soaked for 4 hrs	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)
1	Calf	3	0 1·5	139·5 100·0 = −29 per cent.	6·95 2·54 = −64 per cent.	9·00 0
2	Calf	3	0 0·4	92·0 76·6 = −17 per cent.	3·36 1·09 = −68 per cent.	8·42 0
3	Calf	2	0 0·4	103·5 91·2 = −12 per cent.	4·70 1·38 = −71 per cent.	11·20 3·00 = −74 per cent.
4	Calf	2	0 0·4	131·0 114·0 = −13 per cent.	1·29 1·11 = −14 per cent.	6·00 1·35 = −78 per cent.
5	Calf	1	0 0·6	116·0 113·0 = − 3 per cent.	3·01 0·46 = −85 per cent.	11·30 1·10 = −90 per cent.
6	Young Ox	10	0 1·5	81·0 50·0 = −39 per cent.	5·38 2·06 = −62 per cent.	not measured
7	Young Ox	2	0 0·6	66·0 70·7 = + 7 per cent.	3·12 1·84 = −41 per cent.	8·00 0·90 = −89 per cent.

In some of the experiments the irrigation was stopped after 10 hrs. At this time the two lenses were equally transparent, but the results seen in Table II show that there was a considerable diminution of ATP in the lens in the medium containing glyceraldehyde, and of lactic acid in the lens and surrounding medium.

TABLE II

EARLY CHEMICAL MANIFESTATIONS OBSERVED IN LENSES EXPOSED TO THE ACTION OF GLYCERALDEHYDE

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Glyceraldehyde (g./l.)	Quantity of Lactic Acid (mg./100 g. fresh lens)	Quantity of Lactic Acid (mg./100 ml.) in Liquid in which Lens soaked for 4 hrs	Phosphate readily hydrolysable by ATP (mg./100 g. fresh lens)
1	Young Ox	10	0	78·8	3·20	9·57
			0·6	47·6 = −40 per cent.	2·12 = −34 per cent.	7·32 = −24 per cent.
2	Young Ox	10	0	62·2	3·02	6·13
			0·6	37·2 = −41 per cent.	2·04 = −33 per cent.	
3	Young Ox	10	0	—	—	9·93
			0·6			4·66 = −53 per cent.

(2) MONO-IODACETIC ACID (4 g./l.)

(*a*) *Transparency.*—Clouding of the lens first appeared soon after subcapsular opacities were observed with the slit-lamp, after 2 hrs' perfusion.

(*b*) *Chemistry.*—The lactic acid content in the lens and surrounding medium was considerably diminished in contrast with that in the control. The concentration of ATP in the cataractous lens was also lowered. The amount of phosphocreatine, which was measured only once, was 7·80 mg./100 g. fresh tissue in the control lens, and 2·79 mg. in the cataractous lens (Table III, overleaf).

(3) SODIUM FLUORIDE

(*a*) After only 4 hrs a slight subcapsular clouding was noted with the slit lamp.

(*b*) A considerable fall in the concentration of lactic acid in the lens and surrounding medium was noted, as well as a diminution of ATP in the lens (Table IV, overleaf).

The total potassium in the control lens (measured once) was 2·61 mg.; in the cataractous lens it was 1·86 mg.

(4) PHLORIDZINE (2 and 1 g./l.)

(*a*) The same phenomena were observed as in the preceding experiments, except that the opacities appeared a few hours later.

TABLE III

EFFECT OF MONO-IODACETIC ACID ON CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Mono-iodacetic Acid (g./l.)	Quantity of Lactic Acid (mg./100 g. fresh lens)	Quantity of Lactic Acid (mg./100 ml.) in Surrounding Medium	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)
1	Calf	18	0 4	not measured	1·530 0·319 = −80 per cent.	7·100 5·194 = −27 per cent.
2	Calf	18	0 4	91 82 = −10 per cent.	4·375 1·629 = −63 per cent.	9·336 2·066 = −78 per cent.
3	Calf	8	0 4	83 67 = −20 per cent.	2·681 1·754 = −35 per cent.	10·458 7·602 = −28 per cent.
4	Calf	6	0 4	78 56 = −28 per cent.	3·866 1·010 = −74 per cent.	8·020 4·035 = −50 per cent.

TABLE IV

EFFECT OF SODIUM FLUORIDE ON CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Sodium Fluoride (g./l.)	Quantity of Lactic Acid (mg./100 g. fresh lens)	Quantity of Lactic Acid (mg./100 ml.) in Surrounding Medium	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)
1	Calf	18	0 2	86 73·5 = −15 per cent.	5·32 1·47 = −73 per cent.	6·560 5·060 = −23 per cent.
2	Calf	18	0 2	104 89 = −15 per cent.	3·08 1·73 = −44 per cent.	6·260 2·353 = −63 per cent.
3	Calf	8	0 2	78 58 = −26 per cent.	1·250 0·670 = −47 per cent.	8·158 6·362 = −22 per cent.

(*b*) Only the concentrations of lactic acid and ATP in the lens were measured; the results, similar to those in the previous experiments, are seen in Table V (opposite).

(5) SODIUM MALONATE (2 g./l.)

(*a*) The lesions produced were similar to those found in the four previous experiments, but they appeared very much later—after 24 hours' perfusion.

(*b*) Only the ATP content in the lens was measured; the fall in the concentration in the lens was similar to that in earlier experiments (Table VI, opposite).

TABLE V

EFFECT OF PHLORIDZINE ON CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Phloridzine (g./l.)	Quantity of Lactic Acid (mg./100 g. fresh lens)	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)
1	Calf	24	0 2	100 72 = −28 per cent.	7·500 5·760 = −24 per cent.
2	Calf	36	0 1	108 92 = −15 per cent.	9·840 3·290 = −67 per cent.
3	Calf	48	0 1	130 76 = −34 per cent.	6.382 4·386 = −32 per cent.

TABLE VI

EFFECT OF SODIUM MALONATE ON CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Sodium Malonate (g./l.)	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)
1	Calf	36	0 2	5·13 3·21 = −38 per cent.
2	Calf	36	0 2	9·03 6·27 = −31 per cent.
3	Calf	36	0 2	10·74 4·89 = −44 per cent.
4	Calf	36	0 2	7·71 5·96 = −23 per cent.

(6) FLUORO-ACETIC ACID (1 and 2 g./l.)

(*a*) The opacities were first observed after about 24 hrs' perfusion with sodium malonate.

(*b*) The ATP content of the cataractous lens showed a definite diminution compared with the transparent control lens (Table VII, overleaf).

The concentration of *citric acid* was also measured during five of these experiments, both in the lens and in the surrounding medium. The quantities found in the control and cataractous lenses were equal; in the surrounding medium, on the other hand, the citric acid in the solution containing fluoro-acetic acid was found in a higher concentration than in the control solution.

TABLE VII

EFFECT OF FLUOROACETIC ACID ON THE CATABOLISM OF THE PERFUSED LENS

Experiment No.	Type of Lens	Length of Perfusion (hrs)	Quantity of Fluoro-acetic Acid (g./l.)	Phosphate readily Hydrolysable by ATP (mg./100 g. fresh lens)	Quantity of Citric Acid (mg./100 g. fresh lens)	Quantity of Total Citric Acid (mg.) in Surrounding Medium
1	Calf	36	0 2	9·96 7·83 = −22 per cent.	—	—
2	Calf	36	0 2	10·27 6·27 = −39 per cent.	—	—
3	Calf	36	0 1	13·06 8·94 = −31 per cent.	—	—
4	Calf	48	0 1	10·66 6·69 = −38 per cent.	—	—
5	Calf	48	0 1	—	4·50 —	5·00 7·20 = +31 per cent.
6	Calf	48	0 1	—	5·40 6·20 = +13 per cent.	6·90 8·10 = +15 per cent.
7	Calf	48	0 1	—	6·00 5·10 = −15 per cent.	7·20 9·00 = +20 per cent.
8	Calf	48	0 1	—	5·00 5·30 = + 6 per cent.	6·60 7·50 = +12 per cent.
9	Calf	48	0 1	—	5·65 5·20 = − 8 per cent.	7·20 9·20 = +22 per cent.

Discussion

At which point in the carbohydrate cycle do these substances act?

(1) The action of glyceraldehyde is not completely clear. It is possible that it inhibits the activity of hexokinase, which might activate the combination of l-glyceraldehyde and triose-phosphate, to form l-sorbose-1-phosphate. This substance is very similar to glucose-6-phosphate, which is formed by the phosphorylation of glucose in the presence of hexokinase, and it is to be remembered that synthetic l-sorbose-1-phosphate strongly inhibits the action of hexokinase. If this is true, it would mean that the action of glyceraldehyde affects the first stage of carbohydrate glycolysis.

(2) Mono-iodacetic acid inhibits the action of triose-phosphate dehydro-

genase on the formation of 1-3-diphosphoglyceric acid from 3-phosphoglyceraldehyde.

(3) Sodium fluoride inhibits several reactions in the cycle:

(*a*) phosphatases, which are necessary for the phosphorylation of glucose;

(*b*) adenosine triphosphatase;

(*c*) enolase, the enzyme responsible for the formation of phosphopyruvic acid from 2-phosphoglyceric acid.

(4) The action of phloridzine in inhibiting the phosphorylation of glucose, necessary to allow the penetration of hexose into the lens, suggests that the lens derives its nourishment from an external source. In these circumstances the lens could survive, but only at the expense of its own glucose and those intermediary products which it contains, and only until these reserves were exhausted. It follows that the carbohydrate metabolism is disturbed at the commencement of the cycle.

(5) Sodium malonate inhibits succinic dehydrogenase and prevents the formation of fumaric acid from succinic acid. The aerobic cycle is therefore undisturbed until the succinic acid stage; this substance will accumulate and the catabolic process will cease.

(6) Fluoro-acetic acid inhibits isocitric dehydrogenase, preventing the formation of oxalosuccinic acid from isocitric acid. Citric acid accumulates and the subsequent reactions do not take place.

In the breakdown of sugars, the four first inhibitors act on the enzymes of the anaerobic cycle; with sodium malonate and fluoro-acetic acid, the block is at the level of the citric cycle.

Conclusions

The experiments undertaken have confirmed that a blockage of the breakdown of sugars is always followed by cataract. The first four substances used acted at different phases of the anaerobic cycle; sodium malonate and fluoro-acetic acid on the aerobic phase. Although their site of action is different, all these substances produced marked opacification of the lens. The cataract appeared most quickly when the block affected the enzymes at the commencement of the cycle; less quickly with the agents which disturbed the citric cycle. The positive results of these experiments indicate that the breakdown of glucose in the lens is similar to the process in other organs.

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SUBSTITUTE FUNCTIONS OF THE BLIND AND THE DEAF AND BLIND*

BY

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BLINDNESS was and still is considered the most serious of defects, and of all those suffering from a bodily infirmity the blind are the invalids who are most pitied by their fellow-men. But if you ask those who are both deaf and blind which defect is the most difficult to bear, their answer is without hesitation: deafness. And, indeed, the lack of sight can be offset to such a high degree by the other senses, that a normal and efficiently trained blind person is able to live and to work like a man who can see.

That is what the oculist, who is the first to be asked for advice, ought to know when he can give a patient no hope of retaining his sight, for thus he will be able to help the patient by relieving him of the paralysing fear of impending blindness.

J. W. Klein of Vienna invented in 1804 a primary script for the blind based on capitals shown in relief, and in 1829 Louis Braille of Paris, who was himself blind, gave to the blind their most precious possession, the script based on the 6-dots system which was easier and quicker to read. Teaching the blind then made rapid progress. By means of tin matrices the multiplication of books, maps, and pictures was made possible. Nearly every language has its Braille-shorthand, and big Braille libraries are found in every country; monthly periodicals are produced, and the Braille music-script has made possible the publication of musical scores.

A very important subject is the development of a sense of form by teaching the blind to model objects which they have learned to know by handling them.

There is very little, apart from light and colour which are perceptible only to the eye, that the blind cannot learn. When the well-known American Helen Keller writes of " the sulphur-yellow thunder-sky ", or when a man born blind says " the steeple of our church is reflected in the crystal water of the brook" or speaks of " sky-blue forget-me-nots and dark-blue violets ", these are only correct reproductions of what they have heard and assimilated.

One substitute for the eyes is the sense of feeling, especially in the fingertips, which can be developed to a very high degree. As to myself, I can read Braille well with gloves on, even thick leather ones. It cannot be emphasized

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enough that no finger is too old or too horny to learn to feel accurately. I have taught many people older than 65 years, among them a woman of 75 years and a man of 80, and I also had among the blind of the first world war a patient whose hands were hardened by manual work.

The second substitute function is the sense of hearing. The blind listen far more accurately than those who see, because their sense of hearing is of far more use to them. Sounds speak a different language to the blind, especially the sounds of nature; the wind through the tops of the trees, the waves on the beach, and the peals of thunder. It is significant that in the dreams of the blind these sounds often occur, which is the consequence of their dreaming acoustically.

Through the cooperation of the ear the blind can form a more or less correct image of their direct environment, in which a quick grasp and a good power of combination play an important part. If a blind person goes to the theatre, and his companion describes the scene to him when the curtain rises, he is able to imagine what happens on the stage, and to understand the play.

Like the hand, the human voice can convey fine shades of personality; without asserting that this holds good for every case, we may say that through the voice and the way of speaking a blind man gets to know something about the speaker's features. I have myself experienced the most surprising examples of this.

Though the ear is of great importance in helping the blind to adapt themselves to their surroundings, it lets them down in estimating distances. Tests with others and with myself have convinced me that distances of more than about 10 yards cannot be estimated correctly, and still less in it possible to judge height, as has been proved by tests with church bells, sounds of masonry on different storeys of a building, and other noises from above. Consequently, the blind cannot imagine accurately any extent except when it is relatively small.

It is out of the question for them to form an approximately correct idea of a large square, even when they walk all around it, or of the inside of a theatre. But this does not detract from the importance of the ear for the blind.

The third substitute function is the sense of smell. It is of minor importance, but serves as a good guide in cases when a blind person walks without a companion. In places known to him the smells issuing from different shops are a great help. A blind friend, who came to see me often, found the house, which was the third from a corner with a grocer's shop, by the smell of it, and in another case known to me a baker's shop served the same purpose. The importance of the sense of smell is emphasized by a letter I received from a deaf and blind friend:

> A great misfortune has happened to me, as I have lost my sense of smell. It is only now that I feel really helpless.

The Deaf and Blind

Fortunately there are not too many suffering from this double infirmity, though their number is great enough. Up till now their number has not been correctly fixed by statistics in any country. There are not many persons born deaf and blind, nor many deaf and blind children, for in most cases the deafness occurs later in life.

How do we communicate with these people? When they know Braille, which is often the case, communication is easy. With those who had learned to write before they became blind, one can write in their hand, which they like. But there are other special methods of communication.

The oldest method, no longer in use, is for the deaf and blind person to put the fingertips of one hand on the lips of the speaker and the other hand on the larynx. In this way he is able to recognize the sounds through the difference in movements and vibrations, but this is very difficult and unpleasant to operate.

Of the other existing methods (touch-alphabets) there are two good ones in use:

(1) The deaf and blind person wears a glove on which the characters have been arranged in a manner known to him, and the " speaker " then has to touch any character wanted. In this way the seeing man has nothing special to learn. Much practice brings good results.

(2) Of the other touch-alphabets, which are more or less similar, the Lorm system is the best. It is named after the Austrian poet Hieronymus Lorm (1821–1902), who with his daughter invented this system when he became blind and deaf late in life. The characters are indicated by taps and strokes on the back of the hand or on the palm. It is so simple and clear that after only a little practice a fluent conversation is possible. There is still a very important psychological trait, for the taps and strokes express something individual, just like the voice, and so the deaf and blind person recognizes his companion at the very first characters. For trained " Lormers " there is no difficulty in transmitting and understanding books and newspapers or lectures, or even the conversation of the persons in the room. I myself have often been the interpreter in such cases.

It must be added that the deaf and blind can speak normally, but owing to lack of control their speech usually becomes indistinct.

The above-mentioned resources enable the deaf and blind to achieve a normal mental development.

It is a matter of course that teaching deaf and blind children, who have never had either optical or acoustical impressions, is very difficult, especially at the beginning, and also later on when abstractions have to be explained. This requires great patience on the part of the child, and the system is too intricate to be described here.

But what of the power of observation and the capacity of orientation in cases

where the hand cannot be used as the substitute for the eye and the ear? Now we come to the point of having to treat further details of the sense of feeling. The achievement of the sense of feeling is not based only on the efficiency of the hand and the fingers, but the skin of the entire body can be trained to a very high degree of sensitiveness. This involves a sensitiveness existing for objects in one's immediate neighbourhood. The best name for this faculty is the French *sens de l'obstacle* and the German *Fernempfinden* or *Tiefensinn der Haut*.

The whole matter is not new, for Petrarch and Goethe wrote about similar tests in the dark.

What exactly the *sens de l'obstacle* means, is not yet known to us. The first tests, taken by the teachers Kunz and Truschel of the Institutes for the Blind at Illzach and Strasbourg (Alsace), go back as far as 1886. Both mention the ear and " something else which cannot be defined further ". Later tests even speak of a sixth sense characteristic of the blind. All experiments resulted in proving that the persons had an accurate sensitivity for objects near them. Professor Hanselmann of the Heilpädagogische Seminar at Zürich and Professor Erismann of the Psychologische Institut at Innsbruck have arrived at the same results with their latest tests. They have experimented with blind persons and have correctly concluded that the *sens de l'obstacle* is situated in the ear. But none of their experiments were made with deaf and blind people, as far as I know. I have worked with such persons, in whom the sense of hearing was lacking, and found that they all reacted to objects near them, *e.g.* walls, furniture, trees, and even openings in the wall, etc. This proves the existence of another agent of perception besides the ear. Though psychologists and neurologists have studied this problem, the nature of the *sens de l'obstacle* has not yet been found. Some neurologists mention possible waves in the ether unknown to the normal person. It is a fact that the persons tested acknowledged a sense of oppression. Not long ago a deaf and blind man used the words: " when I *feel* somebody near me . . . . ".

The *sens de l'obstacle* can be situated in any part of the body. As for myself it is strongest in the upper arms, the skull, and the feet. Generally the sensitivity is very strong in the feet. I practised with a blind and deaf girl in Amsterdam, who always held her hands stretched out in front of her, as so many blind persons do, and her movements were very unsteady. When I advised her to hold her hands behind her back and to note the *sens de l'obstacle* of the whole body and especially of the feet, the results were astonishing. All my test convinced me that besides the ear some other sense must function.

It is important to pay attention to the *sens de l'obstacle*, because it influences the movements and attitudes of blind people making them more steady and supple.

Thus the coordination of the substitute functions enables the blind to

adapt themselves to the world of the seeing; they lose the handicap which marks them as " blind ", and are delivered from the isolation which compels them to live in the periphery of society. That is of the greatest importance, as the new methods of care for the blind aim at finding suitable occupations where they can work amongst the seeing as one of them. Besides those pursuing a profession and applying themselves to music, many blind persons work as telephonists and short-hand typists, or as craftsmen in factories. Many women are trained as housekeepers, and learn besides weaving and knitting, to clean, to cook, to sew by hand as well as with a sewing-machine, and even to iron. I myself know several women who perform their task as housekeepers and mothers very well. Even deaf and blind men and women have succeeded in this respect.

It may be possible for the blind to consider their blindness not as an irretrievable calamity, but as a misfortune which can be overcome through the development of the substitute functions, and life is thus made easier to bear and can be more or less successful even for the blind and deaf.

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NEOVASCULARIZATION OF THE DISC IN CHRONIC SIMPLE GLAUCOMA*†

BY

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NEW blood vessels appear on the disc in many ocular conditions, but their appearance in glaucoma is infrequent. Duke-Elder (1940) describes the formation of new blood vessels on the retina and the optic disc due to glaucoma as common, and cites several references from the older literature (Von Graefe, 1854; Hormuth, 1903; Bloch, 1906; Axenfeld, 1911; Kraupa, 1915). Fuchs (1951) also mentions the occurrence of newly formed blood-vessels on or close to the optic disc in glaucomatous eyes. But no reference of the condition in chronic simple glaucoma is found in any recent literature.

In India neovascularization of the retina or disc has been known to occur in epidemic dropsy glaucoma where the fundus often shows retinal haemorrhage. In the Eye Infirmary, Medical College, Calcutta, where large numbers of glaucoma cases are seen yearly, new vessel formations are seldom encountered in conditions other than vascular glaucoma.

Case Reports

Case 1, a married woman aged 58, came to the Eye Infirmary, Medical College, Calcutta, on June 15, 1951, with the complaint of hazy vision in the left eye. She also gave the history of occasionally seeing rainbow haloes around lights in the left eye.

Examination.—Left eye: Visual acuity 6/60, cornea steamy, anterior chamber shallow, disc shallow cupping, tension 40 mm. Hg (Schiötz), visual field marked nasal depression.
Right eye: Visual acuity 6/9, cornea clear, anterior chamber shallow, disc slight physiological cupping, tension 28 mm. Hg (Schiötz), visual field normal.

Therapy.—She was given pilocarpine 1 per cent. drops, but as the tension did not improve, a left trephine was performed on June 28, 1951.

The patient remained well until March, 1952, when she complained of hazy vision in the right eye.

Examination (March 31, 1952).—Tension 30 mm. Hg (Schiötz) in the right eye and 25 mm. Hg (Schiötz) in the left eye.

Therapy.—Pilocarpine 1 per cent. drops were advised for the right eye. One week later she complained of sudden deterioration of vision in the right eye.

Examination.—Visual acuity 6/24, cornea clear, anterior chamber shallow, fundus full of scattered superficial flame-shaped haemorrhages. Blood and urine examination showed nothing abnormal. Wassermann reaction negative. Blood pressure 145/80.

With the usual treatment with Rutin, vitamin C, and iodide, the haemorrhages completely disappeared leaving no trace in 6 months' time.

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Further Developments.—In January, 1953, the patient was seen by Prof. Karl Lindner who found the ocular tension in both the eyes to be within normal limits. His report on the fundus condition was " slight physiological cupping of the disc in the right eye and cupping of the disc with optic atrophy in the left eye ". In May, 1953, the patient came again with the complaint of hazy vision in the morning. The right fundus showed slight physiological cupping of the disc, but on the nasal half there was an anastomotic venous loop. There was no other new vessel formation in any other part of the fundus, and no sign remained of the previous retinal haemorrhages. The left fundus showed besides the cupping of the disc with optic atrophy a very well-marked anastomotic vein on the temporal half (Fig. 1). Had not this patient been under constant observation since the beginning of the illness, the new vessel formations would have been diagnosed as possibly of congenital origin. In October, 1953, the patient had a heart attack, and the eyes were examined a fortnight later. The left fundus condition was as before, but in the right eye was a large patch of haemorrhages with exudates along the inferior temporal vein. The new blood vessels seen on the discs of both eyes showed no further change. When the patient was last examined (January 18, 1954) the haemorrhages and exudates in the right eye had been partially absorbed.

FIG. 1.—Case 1, left eye, showing new vessel formation on disc in chronic simple glaucoma. Disc shows shallow cupping and a venous anastomosis between the central vein and a tributary vein.

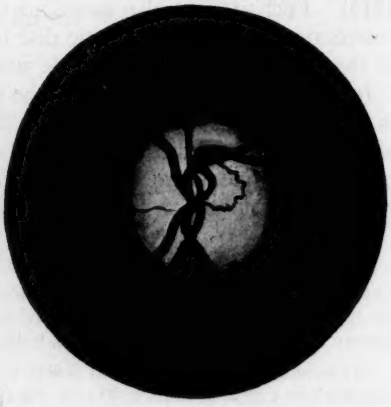

FIG. 1.—Case 1, right eye, showing new vessel formation on disc in chronic simple glaucoma. Disc shows shallow cupping and a venous anastomosis between the central vein and a branch vein.

Case 2, male, aged 61, came to the Eye Infirmary, Medical College, Calcutta on November 6, 1953, complaining of failing vision during the last 6 months.

Examination.—Right, visual acuity finger movement only. *Left,* visual acuity 6/24. In both eyes the anterior chamber was shallow and the ocular tension 49 mm. Hg (Schiötz). Both discs showed cupping with optic atrophy and new vessel formations in anastomotic loops (Fig. 2). In the right eye a communication was found between a small vein arising from the trunk of the central vein and a twig arising from a main branch vein. In the left eye there were two venous communications, one between two nasal branch veins and the other between a temporal branch vein and a twig from the central vein. The neovascularization was limited to the disc, the rest of the fundus being normal.

Blood and urine examinations showed nothing abnormal, the Wassermann reaction was negative, and the blood pressure 145/85.

Therapy.—On November 7, 1953, the left eye was trephined. When the patient was last examined (January 21, 1954) there were no further changes in the vessel formations on the discs, and the rest of the fundi was normal.

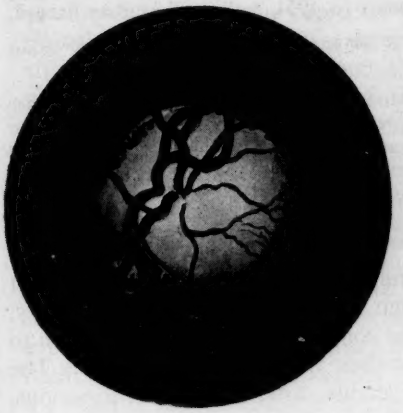

FIG. 2.—Case 2, left eye, showing new vessel formations on disc in chronic simple glaucoma. Disc shows deep cupping and two venous anastomoses, one between two branch veins and the other between a branch vein and a central vein.

FIG. 2.—Case 2, right eye, showing new vessel formation on disc in chronic simple glaucoma. Disc shows deep cupping and a venous anastomosis between the central vein and a main branch vein.

Case 3, male, aged 54, came to the Eye Infirmary on November 12, 1953, with a history of gradual loss of vision.

Examination.—Right, visual acuity 3/60. *Left,* visual acuity finger movements only. In both eyes the cornea was clear, and the anterior chamber shallow. Ocular tension of the right eye was 30 mm. Hg (Schiötz), and of the left eye 35 mm. Hg (Schiötz). The right disc showed glaucomatous cupping with optic atrophy and very marked congenital peripapillary pigmentation. On the temporal half of the disc, there was an anastomotic venous loop with communication between a twig from the trunk of the central vein and a twig from the main branch vein (Fig. 3). There was no neovascularization of any other part of the retina and the rest of the fundus was normal. The left disc showed marked glaucomatous cupping with optic atrophy, but no new vessel formation on either the disc or the retina. There was slight congenital pigmentation on the nasal side of the disc.

FIG. 3.—Case 3, right eye, showing new vessel formation on disc in chronic simple glaucoma. Disc shows deep cupping and a venous anastomosis between the central vein and a main tributary vein. The well-marked peripapillary pigmentation is congenital.

Blood and urine examinations showed nothing abnormal. The Wassermann reaction was negative, and the blood pressure 155/90.

Therapy.—On November 18, 1953, iridencleisis was performed on the right eye.

When the patient was last examined on January 16, 1954, both fundi were unchanged.

Case 4, male, aged 50, attended on October 5, 1953, with the history of loss of vision in the left eye.

Examination.—Right, visual acuity 6/18, fundus normal. *Left,* visual acuity finger movements only, anterior chamber shallow, tension full on digital examination; disc showed marked cupping with optic atrophy and neovascularization in the form of an anastomotic venous loop. The rest of the fundus was normal. No further investigations were made as the patient did not return to the clinic.

Discussion

New blood vessels grow on the disc and the retina either as a manifestation of congenital vascular defect or through ocular diseases of inflammatory, neoplastic, or haemorrhagic origin. The commonest cause is obstruction to the central vein or the central artery or their tributaries or branches. The resultant neovascularization may be venous, arterial, or arterio-venous, according to the nature of the aetiological factor.

The mechanism of their formation in the above conditions is not difficult to understand. It is also easy to understand how the new blood vessels grow on the retina in the secondary glaucoma following thrombosis of the central vein, but it is difficult to explain why new blood vessels form on the disc in chronic simple glaucoma.

In the four cases described above, the new vessels on the disc were veins. The first patient had chronic simple glaucoma in both eyes, and before the appearance of new blood vessels there was extensive retinal haemorrhage in the right eye, the cause of which was unknown. The neovascular formation on the right disc might thus be secondary to the retinal haemorrhage, but there was no apparent reason for the new blood vessels in the left disc, or in the other three cases.

The mechanism at work in all these cases may perhaps be explained as follows: In every case the anastomotic process has one definite pattern. The communicating loop is a vein and the communication is between two veins—either the trunk of the central vein and a tributary vein or between two tributary veins. The site of origin of the communicating twig from the branch vein is always beyond the crossing of the vein by an artery. In glaucoma when there is rise in ocular tension, the pressure effect is transmitted at the arterio-venous crossing on the disc where the already compressed vein is further constricted so that there is partial obstruction to the venous flow. When the obstruction is complete, the fundus picture is that of thrombosis of a tributary vein. But when it is partial and probably intermittent, the obstruction to the vein leads to the formation of a venous shunt which is Nature's attempt to get rid of the block.

As a result of the venous shunt, the blood in the obstructed vein can flow back and empty into the central vein *via* the communicating loop. The process of obstruction will be aggravated if co-existent arteriosclerotic change is already present in the vessel wall. All these four patients were over 50

years old, so that some degree of senile arteriosclerosis could be expected, though no serious change was detected ophthalmoscopically. None had any sign of inflammation in the fundus, and the lesions were not of a neoplastic nature. Except the right eye of Case 1, none had any history of haemorrhage The theory of partial and intermittent venous obstruction due to raised ocular tension is the only likely explanation for appearance of a new venous shunt on the disc.

Summary

Four cases of chronic simple glaucoma are described in which new anastomotic veins were seen on the disc. In one eye of Case 1 the neovascular formation probably had a haemorrhagic basis, but for the rest no aetiological explanation apart from the raised ocular tension due to glaucoma presented itself. The possible mechanism of the neovascularization of the disc through the effect of raised tension is described.

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ERYTHROMYCIN IN TRACHOMA*

BY

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ERYTHROMYCIN is a new antibiotic produced by a strain of *Streptomyces erythreus*. The clinical indications for the drug are as yet undetermined. It is said to be effective against Gram-positive cocci, Gram-negative cocci, the *Clostridium* group, anthrax, *Haemophilus pertussis*, and Rickettsiae and certain viruses.

Material and Methods

A series of 100 patients with trachoma in the infiltrative or follicular stage, in which inclusion bodies could be seen, was selected for this study. Conjunctival scrapings were obtained from the upper fornix by a sharp curette and spread on a slide, care being taken that no blood oozed out. The scrapings were stained by methylene blue and citric acid stain according to the technique of Poleff (1952), who recommends that the smear should be stained for 3 minutes. We found that the smear should be stained for 4 minutes to get good results.

Fifty cases were used as controls to whom no treatment was given except normal saline drops (Agarwal and Gupta, 1954).

Fifty cases were given erythromycin tablets 100 mg. 4-hrly for a week, with local application of ointment in concentration of 5 mg./g. two to three times a day.

A search for inclusion bodies was made in stained slides every 2 weeks. The treatment was continued in several cases even after the inclusion bodies were absent from the smears. The treatment was continued for 6 weeks and final examination and assessment was made at the end of this period. The presence and progression or retrogression of pannus was also recorded during the period of observation. Such subjective symptoms as photophobia, redness, discharge, irritation, and gritty sensation were also taken into account and the effect on them of the drug was noted.

Results

Untreated Cases.—Inclusion bodies were present in all four specimens of tissue scrapings in all cases; this confirmed our previous finding that inclusion bodies did not disappear without treatment. The subjective symptoms did not improve.

Treated Cases.—The subjective symptoms started improving within 24 hours and disappeared within 3 days. The pannus retrogressed in 50 per cent. of the cases and in these the inclusion bodies also disappeared (see Table).

Toxicity.—In three cases the local application of erythromycin ointment caused a reaction which manifested itself either in heaviness or swelling of the lids or in conjunctival congestion. In one case an eczematous reaction was seen. In only one case out of fifty was a gastro-intestinal reaction in the form of mild diarrhoea observed. In these five cases treatment was discontinued.

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TABLE

RESULTS OF TREATMENT BY ERYTHROMYCIN

Cases Treated	Clearance of Secondary Infection	Improvement of Secondary Symptoms	Disappearance of						Per cent. Cured
			Pannus			Inclusion Bodies			
			2 wk	4 wk	6 wk	2 wk	4 wk	6 wk	
50	24 hrs	24 to 72 hrs	2	11	12	6	9	10	50

Discussion

The search for a suitable antibiotic or chemotherapeutic drug for the effective treatment of trachoma continues, although quite satisfactory results have been obtained by the use of sulphacetamide and other sulphonamides.

In view of the variable responses to various drugs it is thought that either the sensitivity of trachoma virus to various therapeutic agents is not uniform, or there is more than one strain of trachoma virus.

The response to erythromycin indicates that it is quite an effective agent against trachoma virus as shown by the disappearance of inclusion bodies from smears in 50 per cent. of cases. This series also shows that erythromycin is a quick-acting drug, as in many cases the inclusion bodies had disappeared when the second scraping was taken, *i.e.* in the second week.

The subjective symptoms showed uniform response and the pannus retrogressed in the cases which responded to this therapy. In a few cases, which have been labelled as negative, the subjective symptoms were relieved and the pannus showed some degree of retrogression, but the condition did not completely resolve. If the treatment had been continued for a longer time, better results might have been obtained. Erythromycin has proved worth a trial.

Summary

(1) The study of 100 cases was controlled by the demonstration of inclusion bodies in conjunctival scrapings at intervals of 2 weeks.

(2) Erythromycin was found to be quick-acting and effective in 50 per cent. of cases.

(3) Oral therapy (42 tablets of 100 mg. each) combined with local ointment (5 mg./g.) is recommended.

The authors wish to express their thanks to Eli Lilly and Co., Indianapolis, 6, Indiana, U.S.A., for the supply of erythromycin (Ilotycin, Lilly).

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CORRIGENDUM

It is regretted that in a previous report from this department (*B.J.O.*, **38**, 119) Dr. M. A. Shah was misquoted as stating that aureomycin was useful against trachoma. He has informed us in a personal communication that he has found aureomycin ineffective in this condition.

Brit. J. Ophthal. (1954) 38, 692.

TERRAMYCIN IN TRACHOMA

BY

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TERRAMYCIN, which was discovered by Finlay and his collaborators (1950), was isolated from *Streptomyces rumozus*. The first experiments with it were made at the Mayo Clinic, Rochester, Minn., U.S.A., and it was found to produce an effect upon Gram-positive and Gram-negative bacteria, Rickettsiae, and viruses.

Reports in the Literature

Comparatively few papers have been published on the results achieved by treating trachoma with terramycin, but Bietti (1953), Bengisu Naci (1952), and Mitsui (1951) have published the results of their researches. The Japanese have been the most frequent users of terramycin in trachoma. Mitsui and others (1951) administered this antibiotic in seven hundred cases, 80 per cent. of which were reported to have been cured. These clinical findings were corroborated by their laboratory work. Inclusion bodies disappeared after a few days; histopathological analyses showed improvement; pannus disappeared after 6–10 days. Bengisu Naci (1952) treated ten patients with terramycin capsules, drops, and ointment, and later treated a hundred children, administering terramycin ointment five times a day. Laboratory and clinical control was introduced before and after the treatment. Bietti (1953) treated 206 eyes with terramycin, and thought that it influenced the virus. Good results with terramycin were obtained by Izzet (1951) in Turkey, and by Geraci (1951) in Italy. Rais (1950) investigated cases of pure trachoma and also cases in which trachoma was combined with conjunctivitis. Naccache (1953) treated 38 patients by oral administration and locally, without any toxic or allergic symptoms. Siniscal (1952) asserted that terramycin produced an effect only in cases of superinfection. Very good results were achieved by Town (1951) and Thygeson (1951), and moderate results by Focosi (1953), Lepri (1951), and Caterini and De Vincentiis (1951).

Present Research

Having investigated the results of treating trachoma with the sulphonamides, penicillin, and aureomycin, we decided to apply terramycin and observe its effect upon trachoma in the province of Vojvodina, Jugoslavia.

Material.—We treated eighty patients with terramycin. Our research began on October 1, 1952. The cases were classified in four stages according to MacCallan (1936). We had seven cases in Stage I, forty in Stage II, and 33 in Stage III. 59 of the patients were under 20, eight between 20 and 30, and thirteen over 30 years of age. We chose patients who had not been treated previously, and those in whom the trachoma process was not old-established, so that most of them were in a progressive stage of the disease. Clinical observation was carried out by means of a biomicroscope or a loupe. Microbiological and histopathological examinations enabled us to see the effect produced on the trachomatous process itself. Some of the patients stayed in hospital for 2–3 months, and others were segregated in a home or boarding-school for trachomatous children, but most of the latter group were also treated in hospital for some time.

The patients were divided into two groups: one was treated locally with terramycin, and the other received sulphonamides, besides local therapy. All the cases, with few exceptions, were under our supervision even after the termination of treatment. In all the hospitalized cases, before the actual treatment was begun, a general examination was made. The conjunctival flora was examined in each case, and preparations of conjunctival scrapings were taken. These examinations were made frequently in the course of the treatment, and once a month or once in 2 months thereafter. In order to examine the influence of the drug on the pathological process, we made histopathological examinations, trying to find out whether, even a long time after treatment had been stopped, the pathological process still existed. Sections were taken from the upper palpebral conjunctiva, and, having been fixed in Zenker, were stained with haematoxylin and eosin or by Van Gieson's method. These were taken before and after treatment, and in seven cases also after an interval of 2–4 months. 140 sections were made from 54 treated eyes.

Clinical Features.—The peculiarity of trachoma in Vojvodina is the rare incidence of acute cases. A chronic, follicular, form of the disease, without discharge, is prevalent, and during the last 20 years it has been occurring in a very mild form. A developed pannus and damage to the eyelids are extremely rare in younger persons. The number of cases of pure trachoma is large. A fine diffused infiltration, a few follicles, opaque and differing in size, and still fewer papillae, are generally found in Stage I cases. The process begins in the upper tarsal conjunctiva, near to the free border of the tarsus or on the semilunar fold, where two or three follicles are usually aggregated. There is no discharge. In Stage II a diffused infiltration develops, there are often many opaque follicles, different in size and sometimes aggregated. There is some papillary hypertrophy, but no roughness. The process gradually penetrates deeper into the tarsus, covering the whole tarsal conjunctiva and the upper conjunctival fornix. There are follicles in the bulbar conjunctiva, especially in the upper part. Sometimes there are signs of an initial pannus in the limbus in the upper part with superficial infiltration 1 mm. wide and initial superficial vascularization. Pannus is rarely developed, but if it occurs, the infiltration seldom penetrates deeply. In most of the Stage III cases some fine scarring is to be found. In a small number of cases scarring is prevalent, opaque follicles being found here and there with the infiltration and papillary hypertrophies, and the tarsus being infiltrated and thickened. In such cases pannus is developed and often involves the whole cornea, with deep penetration, and vision is very poor.

Treatment.—In 41 cases the treatment was exclusively local. Ointment was applied six times a day. In 39 cases the patients also received sulphathiazole tablets by mouth. There was little change in the clinical appearances in the first month of treatment, except that in the Stage I cases one had an impression that the diffused infiltration had become smaller, especially under combined therapy. In the second month, besides the regular oral treatment, the antibiotic was administered locally by massage once a day. During the second, and, in more serious cases, during the third month, the diffuse infiltration gradually disappeared, and the follicles and papillary hypertrophies became smaller and then vanished. In a number of cases fine scarring remained, while in others the process was completely cured without scarring. In Stage II regression was slower, and in Stage III it was very slight, but it frequently occurred without any new scarring.

After the termination of the treatment the conjunctivae were pinkish-grey, thin, and smooth, sometimes with fine scarring on the surface, and sometimes without. In Stage II cases some follicles and papillary hypertrophies remained.

The effect on the pannus was favourable. We treated only eleven patients with pannus; the subjective irritation rapidly ceased, hyperaemia disappeared after 2–5 days, the conjunctival infiltration was resorbed within 5–10 days, and after a month the pannus was resorbed completely. After the termination of the treatment vascularization persisted on the corneal surface; this was very rare, but there was scarring in the long-standing cases.

Vision was considerably improved in all cases, and terramycin was seen to influence the true trachomatous pannus.

Of eighty patients, 37 (46·25 per cent.) were clinically cured: of seven Stage I cases, four (57 per cent.); of forty Stage II cases, 24 (60 per cent.); and of 33 Stage III cases, nine (27 per cent.). However, in some cases the pathological changes did not quite disappear even after 3 months' treatment. Follow-up examinations showed that there was a further regression of pathological changes, and so far no case has relapsed. Terramycin combined with sulphathiazole produces quicker and better effects than when it is administered locally only. In general, the more superficial the process the sooner it is cured.

Biomicroscopical Investigation

Before treatment the conjunctival surface in Stage I cases is uneven, diffused, opaque, and opalescent. Longitudinal blood vessels and the tarsus are transparent. The papillae, with a characteristic perpendicular vascularization, in the form of a bouquet, are a little increased and infiltrated, and less transparent, and form groups, causing the uneveness of the conjunctival surface. The papillary hypertrophy is greater near the conjunctival fornix. Here and there small follicles can be seen; they are whitish-grey, transparent, and not vascularized at first, but later fine capillaries can be seen on the surface. This state is directly followed by cicatrization, and fine scarring is formed, but in some cases follicles disappear without any residual scarring.

In Stage II the opalescence is greater. Some longitudinal blood vessels can be seen dimly; there are many papillary hypertrophies, the bouquet of blood vessels is very developed, and infiltration is greater. Among the papillae are seen whitish-grey follicles, hemi-ampullar in form and non-

transparent, their surface covered with a loose net of blood vessels. Most of them are near the canthi and in the conjunctival fornix. Sometimes there is an enormous number of follicles, so that the conjunctiva has a gelatinous look. During treatment the follicles diminish gradually, become clear and white, lose their hemi-ampullar appearance, become transparent and vanish. Fine scarring is formed, and whitish lines can be seen. The papillae become flat and disappear gradually. In the cases considered as clinically cured, the conjunctiva is light, with a smooth surface, transparent, vascularization is parallel to the surface, and there are newly-formed vessels in front of and behind the fine surface scarring.

In the majority of our Stage III cases cicatrization was initial, so that biomicroscopically there was no significant difference between them and the Stage II cases. In a smaller number of cases the conjunctiva was covered with a net of fine linear scarring, sometimes forming islets with a smooth surface. Generally, blood vessels are no longer perpendicular, but parallel to the surface, behind the scars. The papillae are flat and smaller in size. The inner blood vessels can be seen. There is a fine greyish, diffused infiltration. A small number of regressing follicles can be found on the tarsal conjunctiva, especially laterally and in the conjunctival fornix. New blood vessels develop from the inner or conjunctival fornix vessels, forming a dense, superficial net. Regression and cicatrization progress during treatment. In the bulbar conjunctiva, hyperaemia and infiltration are continued into a more or less developed pannus. As for the pannus, the limbus area is infiltrated, the papillae are small, and blood vessels form a bouquet. The direct branches of the foremost conjunctival vessels penetrate into the infiltration, by which they are covered. In the distal part of the limbus can be seen round follicles, surrounded by fine blood vessels. Some of their branches cover the surface of the follicles, and there are many maculae and papillae. During treatment the infiltration is resorbed, and instead of the follicles, fine pits are formed. Vascularization is persistent.

Microbiological Investigation

In all the cases before treatment, often during the treatment, and at intervals after discontinuing treatment, the conjunctival flora was examined and preparations stained by the method of Lindner (1927) and Poleff (1951) were made from the conjunctival scrapings. Before treatment we found inclusion bodies in five of the seven Stage I cases, in thirty of the forty Stage II cases, and in eight of the 33 Stage III cases. We thus found them in 43 out of eighty cases (54 per cent.). After treatment we found them only in two Stage I cases, four Stage II cases, and one Stage III case. During the follow-up period, 2–4 months after the termination of the treatment, they were not found at all. The conjunctival flora became sterile within 2–3 days after the treatment was started. There had been many epithelial cells, which in the course of the treatment and after its discontinuance became gelatinously

degenerate; their nucleus could not be stained and they disappeared gradually. We found Prowazek-Halberstädter bodies, initial and elementary, in the epithelial cells. Pastille and rickettsoid bodies, Leber's cells, small lymphocytes, and erythrocytes were also found.

Since the trachoma bodies disappeared in almost all cases, this could be taken as a proof that terramycin destroyed the virus. However, the fact that the inclusion bodies were found in 54 per cent. of the cases suggests that the virus may exist in an invisible form.

Histopathological Investigation

Histopathological analyses of sections taken before treatment from patients with progressive trachoma (Stages I and II) show papillary excrescences lined with epithelium on the conjunctival surface. In the subepithelial tissue, which is the basis of these formations, and also in the submucosa, there is some infiltration of lymphocytes and plasma cells, usually diffused and more or less intensive. This infiltration includes separate follicles or their conglomerates, composed of bigger or smaller lymphoid elements. Considerable hyperaemia can be seen in the same tissue. The more advanced cases show proliferation of conjunctival elements, occurring either around small blood vessels or in the follicles themselves, with here and there subepithelial cysts. In some cases there is also infiltration among the acini of the lacrimal gland.

After therapy, in a number of cases, especially those in the initial stage, a complete or partial resorption of infiltration occurs (Figs 1-6).

FIG. 1.—Case 18, biopsy before treatment. In the subepithelial tissue of the conjunctiva, beside a diffuse infiltration of lymphocytes and plasma cells, is a large follicle showing signs of necrosis in the middle; above it, the epithelium of the conjunctiva is partly thinned and partly missing.

FIG. 2.—Case 18, biopsy after treatment (after 89 days). The epithelium of the conjunctiva is stratified, lining the low papillae. Subepithelial and pretarsal tissues are compact; separate lymphocytes can be seen. A fat infiltration can be seen in the pretarsal tissue.

FIG. 3.—Case 2 before treatment. Papillary growth with infiltration of lymphocytes, plasma cells, and follicles.

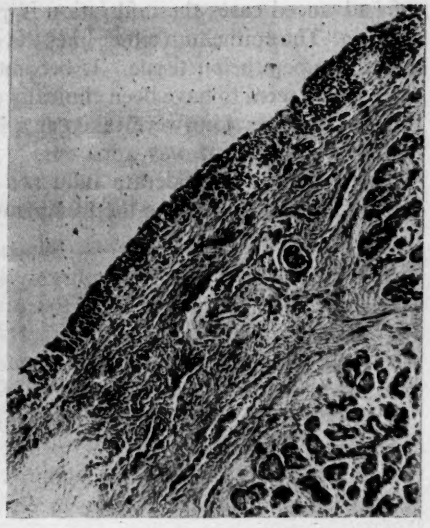
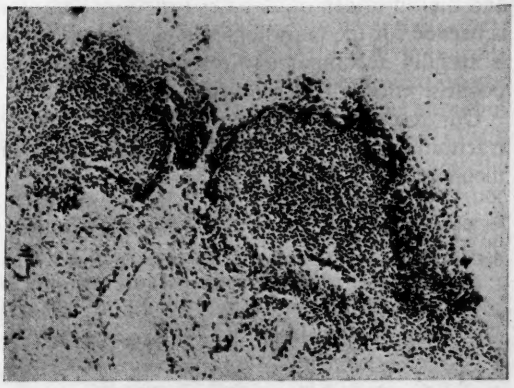


FIG. 4.—Case 2 after treatment (after 62 days). Epithelium stratified; in the subepithelial tissue rare separate lymphocytes can be seen, the tissue itself being compact.

FIG. 5.—Case 4 before treatment. In the subepithelial tissue of the conjunctiva there are follicles, on the periphery around them the beginning of a proliferation of the conjunctival elements can be seen. Under the follicles there are rather widened blood vessels.



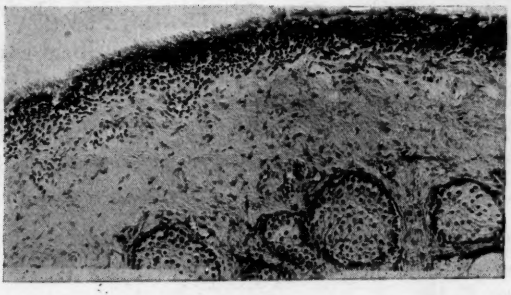


FIG. 6.—Case 4 biopsy after treatment (after 62 days). In the subepithelial tissue, which has become compact, a moderate infiltration of lymphocytes and plasma cells can be seen.

In advanced cases the infiltration is partly resorbed and there is moderate scarring. The epithelium either lines the papillary growth or penetrates deeper into the subepithelial tissue. It becomes metaplastic and stratified. Many cases which seem to have been clinically cured, show only slight improvement. In some cases sections were taken at a longer interval after treatment, when further improvement was apparent.

There is only a moderate influence on the diffuse infiltration and the follicles, probably because the treatment was administered without massage.

Summary

Terramycin used locally favourably influences the trachomatous process, especially when combined with the oral administration of sulphonamides. Its influence on the trachomatous process is more efficacious in new cases when the tissues have not been deeply penetrated. In an advanced case at least 2 or 3 months of treatment are required.

Terramycin has a favourable effect on the pannus.

Of eighty patients, 37 (46·25 per cent.) were clinically cured, and the remaining 43 (53·75 per cent.) improved. In 39 cases, besides the local therapy, sulphonamides were given orally.

The microbiological examination indicates that the trachoma bodies disappeared during treatment in almost all cases. The histopathological examination proves that in nineteen out of 34 patients, from whom biopsies were taken after the termination of the treatment, an improvement was seen, and that in fifteen other cases the result was almost as good. A longer time is needed for the pathological signs to regress, but the fact that the regression is usually accompanied by some fine and slight cicatrization, proves the positive effect of terramycin.

Our research does not indicate that terramycin has a specific effect on trachoma, but combined with sulphonamides and aureomycin, it is a useful medicament.

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CASE NOTES

METASTATIC CARCINOMA OF THE IRIS*

BY

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THE first record of this rare condition is that of Proctor and Verhoeff (1907), who made the diagnosis on iris biopsy without histological examination of the whole eye. The unique case of bilateral metastases reported by Toulant (1916) and the second case of Bollack and others (1927) were diagnosed clinically and no histological examination was made. More precise information is available about the first case described by Bollack and others, in which the diagnosis was established by iridectomy during life; the eye was sectioned after death and contained no other malignant deposit. In the case reported by Larsen (1933), the tumour was removed by iridectomy *post mortem*, but the whole eye was not examined. Hudson and Lister (1934) described a "hypernephroma" confined to the pupillary portion of the iris in a patient from whom a kidney containing a malignant encapsulated growth had been removed 2 years previously. The histology of the ocular tumour strongly suggested its origin from a clear-celled adenocarcinoma of the kidney. The iris tumour in the case reported by Sanders (1938) was histologically demonstrated to be confined to the iris, but no *post-mortem* examination was possible and the primary growth was not discovered, although either bronchus or breast was thought to be its most likely site. Asbury and Vail (1940) claimed that their case was the first in which both the eye lesion and the primary tumour had been studied and compared. Sautter (1948) described an unusual case in which the primary growth, situated above the epididymis, was composed entirely of epithelial cells some of which showed squamous metaplasia. The origin of the tumour remains in doubt but may have been from the epididymis or vas deferens. Reese (1951) refers to two cases personally observed but presents details of only one, and in this the metastatic focus, from a gastric primary, was apparently confined to the iris. The iris tumours in the cases reported by Paufique and Etienne (1951) and Holm-Pedersen (1952) were treated by irradiation and no histological examination of the eye was made.

The number of cases so far recorded in which it has been histologically verified that the metastatic tumour was confined to the iris alone is six. Among 45 cases of secondary uveal carcinoma recorded in the archives at the Institute of Ophthalmology (1935-54) are five in which the iris was

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involved. In only two cases, which it is the purpose of this paper briefly to describe, was the secondary growth confined to the iris.

Case Reports

Case 1, male, aged 67 years (case of Mr. R. C. Davenport), attended Moorfields Eye Hospital in December, 1949, complaining of a " gritty " feeling in the right eye for 2 days. Examination revealed a fleshy, vascular, translucent tumour of irregular outline, filling the angle at 9 o'clock. There was little evidence of inflammation and no cells were seen in the anterior chamber. General examination failed to reveal a primary growth and *x* rays of the chest were normal. The mass in the iris increased rapidly in size and large vessels appeared on its surface, fine keratic precipitates developed, and within a month the eye had to be enucleated for increasing pain. Post-operatively the patient developed an enlarged liver and became deeply jaundiced. He died, at home, one month after enucleation and two months after his initial complaint. No *post-mortem* examination was made.

Ocular Findings.—The eye was fixed in 10 per cent. formalin, opened horizontally, and embedded in celloidin. Macroscopically, a greyish-white mass was seen to fill the temporal filtration angle and spread over the surface of the iris on that side. The retina was detached. Section (Fig. 1) showed an unencapsulated, cubical-cell adenocarcinoma occupying the outer one half of the temporal iris, encroaching on the anterior aspect of the ciliary body, and infiltrating the tissues of the angle and corneo-scleral meshwork. The malignant cells, which had abundant rose-pink cytoplasm and large well-demarcated leptonuclei, were supported by a delicate fibro-vascular stroma and formed a compact pattern of tubules. Mitotic figures were numerous and large areas of necrosis were evident Beyond a few fine keratic precipitates there was no evidence of inflammation in the eye. The histological structure of the growth gave no indication of its primary source but the lung or thyroid were suspected.

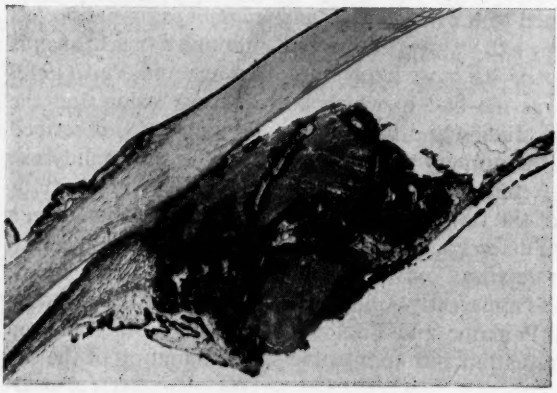

FIG. 1.—Metastatic adenocarcinoma in the iris. Haematoxylin and eosin. ×15.

Case 2, male, aged 76 years (case of Mr. Maurice Whiting), developed pneumonia in December, 1952. In February, 1953, his right eye became painful and a small white nodular mass was seen in the nasal periphery of the iris at about 3 o'clock. Examination of the chest revealed a left bronchogenic carcinoma. The iris tumour enlarged and became more vascular but there were no signs of iritis. The patient died in September, 1953, and at *post-mortem* examination a hard infiltrative tumour was found in the upper zone of the

right lung, numerous metastases being present in the liver. Unfortunately, no histological examination of the pulmonary tumour was made.

Ocular Findings.—The eye was fixed in 10 per cent. formalin, opened horizontally, and embedded in celloidin. Macroscopically, a pinkish-white mass was visible in the periphery of the anterior chamber on the nasal side. Section (Fig. 2) showed that the peripheral iris was replaced by a ragged, partially necrotic, unencapsulated carcinomatous mass extending through the tissue of the angle and into the corneo-scleral meshwork. The growth, which had erupted through the pigment epithelium of the iris so that its posterior surface was in contact with the capsule of the cataractous lens, was composed of polygonal and spindle-shaped cells of moderate size, arranged in irregular sheets without glandular pattern. Mitotic figures were numerous, and the stromal network minimal. Fine keratic precipitates were evident, and a diffuse plasma cell infiltration was present throughout the iris, upon the anterior surface of which a well-marked fibro-vascular membrane had formed. The episcleral tissues over the growth were densely infiltrated with small lymphocytes.

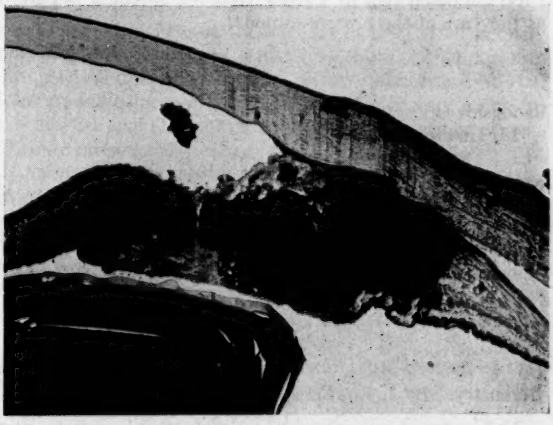

FIG. 2.—Metastatic bronchogenic carcinoma in the iris. Haematoxylin and eosin. ×15.

Summary.

The clinical and pathological findings are recorded of two cases of metastatic carcinoma confined to the iris, one from the lung and the other from an undiscovered primary source. The literature is briefly reviewed.

My thanks are due to Mr. R. C. Davenport and Mr. Maurice Whiting for permission to publish their cases and to Dr. Alexander Ward for clinical details of Case 2. I am indebted to Dr. P. Hansell for the photomicrographs and to Dr. Norman Ashton for advice and criticism.

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CORRESPONDENCE

EXTRA-CONJUNCTIVAL IMPLANTS

To the Editorial Committee of the BRITISH JOURNAL OF OPHTHALMOLOGY

SIRS—Mr. Choyce has had the kindness to read my article. I would have appreciated his criticism all the more had he read it more carefully.

His choice of the word "disservice" is unfortunate and unjustified. This is a new departure in the technique of implants, with a minimum of foreign material buried under conjunctiva, in an attempt at preventing sepsis and extrusion.

My list of thirteen cases, dating from March, 1953, fully justifies further trial of this technique, inasmuch as, so far, there is no sign of sepsis or extrusion in any of them. I feel confident that in 3 years' time the implants will still be *in situ*, in sockets as clean as they are at the present moment.

Yours faithfully,

M. L. NAIRAC.

BROOKSIDE HOUSE,
38, THORNHILL GARDENS,
SUNDERLAND.

September 17, 1954.

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CHOYCE, D. P. (1954). *British Journal of Ophthalmology*, **38**, 575.
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BOOK REVIEWS

Perimetry. By J. ZUCKERMAN. 1954. Pp. 391, 156 figs. Lippincott, London. (80*s.*).

This comprehensive treatise on perimetry introduces certain novel features. The full technique of visual field examination is described in detail, together with the anatomical features of the whole visual pathway. General information about the aetiology and symptomatology of the various abnormalities described is included as space allows, to clarify the perimetric features. The author feels that the clarification of the text requires considerable repetition of both descriptions and diagrams, which is valuable from the point of view of the student. Similarly, many of the Tables are most useful for classifying facts in the reader's mind as well as for ready reference.

The anatomy of the visual pathway introduces the "Zuckerman Cross" to assist in the identification of the various parts of the visual connections, but it seems doubtful whether this makes matters more simple or merely provides an added complication. The "Zuckerman Cross", which suggests standardization of the methods of indicating the isopters and scotomata, both for white and colour, appears to be a real advance, and might, if generally adopted, save much time and trouble.

The book is clearly presented, but there is too little contrast between the print of the text and that of the description of the diagrams.

This is a book which should be read by all ophthalmologists and neurologists, and general physicians will also find much to interest them. Students, in particular, will find it valuable, as it presents a simple account of modern perimetric practice and emphasizes its importance in both diagnosis and prognosis.

The Practice of Refraction. Sixth edition, 1954. By SIR STEWART DUKE-ELDER. Pp. 335, 239 figs. Churchill, London. (21*s.*).

The main difference from the former editions lies in the addition of a chapter on contact lenses. Written in the author's inimitable style which makes all his books so readable, this book makes it easy for the refractionist to acquire a very thorough working knowledge of the subject. If he absorbs all that is placed before him, there will scarcely be a problem in the consulting-room that he will not be adequately fitted to solve. The chapter on contact lenses is very useful at a time when these optical aids are being made by people outside the recognized profession. Since the newspapers are advertising contact lenses under "favourable hire-purchase terms", it behoves every oculist to make himself acquainted with their construction, optics, suitability, and limitations, and all these he will find in this very instructive book.

May and Worth's Manual of Diseases of the Eye. Eleventh edition, 1954. Edited by T. K. LYLE and A. G. CROSS. Pp. 724, 305 figs (32 col. pl.). Baillière, Tindall, and Cox, London. (35*s.*).

The eleventh edition of May and Worth's "Manual of Diseases of the Eye" has been rewritten and enlarged by new collaborators, Lyle and Cross, both of whom are surgeons at Moorfields, Westminster and Central Eye Hospital. According to its preface it is written for the undergraduate medical student, for those who are going to specialize or whose general medical work includes ophthalmology, and for senior nurses studying for diplomas in ophthalmic nursing.

As an introduction to ophthalmology for those who are going to specialize this text-book is particularly well designed. It tells in lucid language how to examine the eye, diagnose, and treat its diseases. There are some valuable chapters for the serious student who wants to know the relationship of ophthalmology to general, neurological, and psychological illness, for this marginal territory is a real difficulty to the novice who knows neither how nor whence to inform himself. These chapters provide a reliable scaffold of knowledge which can be enriched in time by wider reading and from personal experience.

There is a decided and welcome neurological bias in the planning and spacing of the material, in that separate chapters are devoted to visual field defects, the pupils, and nystagmus. There are also helpful chapters on amblyopia, ophthalmology in the tropics (by E. J. Somerset), and an up-to-date and practical summary of ocular therapeutics. A comprehensive index makes the volume a useful source of reference for the general practitioner or for the harried examinee.

The book is clearly printed and pleasantly sub-headed and the proofs have been carefully read. The line-drawings, photographs, and coloured fundus paintings are excellent, but some of the coloured plates of the external diseases have probably served their time and might be improved (*e.g.*, Plate X, Fig. 2) without detracting from the continuity of later editions. The book can be thoroughly recommended as a practical and orthodox survey of present-day ophthalmology.

Tuberculoses Oculaires et Tuberculoses Paraganglionaires (Ocular and "Paraganglionic" Tuberculosis). 1953. By L. Paufique, P. Bonnet, and J. Brun. Pp. 186, 43 figs. Masson, Paris. (1,350 *frs*; 30*s.*).

This monograph, based on statistics of 740 cases of ocular tuberculosis (not including cases associated with miliary tuberculosis or tuberculous meningitis), discusses all aspects of the condition. The contrast is drawn between lesions due to Koch's bacillus and those which result from the patient's sensitivity to tuberculous toxins. The difficulties of diagnosis are emphasized, and the necessity for the careful interrogation of patients to ascertain whether there is a personal or family history of tuberculosis,

or whether the patient has been in contact with any other tuberculous subject. The primary infection, which usually involves the mediastinal glands, is described and the spread of the infection to other organs of the body. The ocular involvement is divided into early and late types, and includes phlyctenular kerato-conjunctivitis, deep keratitis, and uveitis. The differential diagnosis of ocular tuberculosis is considered, and treatment is described. The second section of the monograph is devoted to tuberculosis of the lymphatic glands and to the relationship of this condition to ocular tuberculosis. Radiotherapy is advised for tuberculous lymphadenopathy and details of the methods of treatment are given.

NOTES

Midland Ophthalmological Society

Session 1954-1955

November 23, 1954, 3 p.m., Derbyshire Royal Infirmary, London Road, Derby.

March 15, 1955, 3 p.m., Coventry and Warwickshire Hospital, Stoney Stanton Road, Coventry.

May 21, 1955, Joint meeting at Sheffield with the North of England Ophthalmological Society (details later).

June 10, 1955, 3 p.m., Shrewsbury Eye, Ear, and Throat Hospital, Murivance, Shrewsbury.

September 30, 1955, 2 p.m., Birmingham and Midland Eye Hospital, Annual General Meeting, including the Middlemore Lecture.

November 25, 1955, 3 p.m., Oxford Eye Hospital, Walton Street, Oxford.

OBITUARY

William Henry Simpson

The death occurred at his home in Wellington on July 28, 1954, of Dr. William Henry Simpson, a veteran of both world wars and one of the leading eye specialists in New Zealand. He was educated at Otago and Edinburgh Universities and completed his training as a house surgeon at Moorfields. He was associated with the Wellington Hospital from 1922 until his retirement last year. He is survived by his widow and one son, Dr. Derek Simpson, who is in practice as an ophthalmic surgeon in Vancouver, B.C.

Corrigendum

British Journal of Ophthalmology (1954), **38**, 637, l. 6: for "does prove" read "does not prove".